AIR FORCE HEALTH STUDY

FINAL REPORT

An Epidemiologic Investigation of
Health Effects in Air Force Personnel
Following Exposure to Herbicides

VOLUME I

1997 Follow-up Examination Results
May 1997 to February 2000

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13. ABSTRACT (Maximum 200 words)

This report summarizes results from the Air Force Health Study (AFHS). The AFHS is an epidemiological study to determine whether adverse health effects attributable to exposure to herbicides exist in veterans of Operation Ranch Hand. Operation Ranch Hand was the unit responsible for the aerial spraying of herbicides, including Herbicide Orange, in Vietnam from 1961 to 1971. A Comparison cohort comprised Air Force veterans who served in Southeast Asia during the same time period that the Ranch Hand unit was active and who were not involved with spraying herbicides. The summarized data were collected during a physical examination administered between May 1997 and April 1998. Of 1,149 eligible Ranch Hands, 870 (75.7%) participated and of 1,761 eligible Comparisons, 1,251 (71.0%) participated. Statistical analyses assessed differences between Ranch Hands and Comparisons and associations between health-related endpoints and extrapolated initial dioxin, dioxin exposure category (Comparisons, background Ranch Hands, low Ranch Hands, high Ranch Hands), and dioxin measured in 1987. The study has insufficient statistical power to assess increases in the risk of rare diseases, such as soft tissue sarcoma. Diabetes and cardiovascular abnormalities represent the most important dioxin-related health problems seen. From a public health perspective, these two areas demand the greatest attention.

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NOTICE

This report presents the results of the 1997 follow-up of the Air Force Health Study, the fifth examination in a series of epidemiological studies to investigate the health effects in Air Force personnel following exposure to herbicides. The results of the 1982 baseline study, the 1985 follow-up study, the 1987 follow-up study, and the 1992 follow-up study were presented in five reports: the Baseline Morbidity Study Results (24 February 1987), the Air Force Health Study First Followup Examination Results (15 July 1987), the Air Force Health Study 1987 Followup Examination Results (16 January 1990), the Air Force Health Study Serum Dioxin Analysis of 1987 Examination Results (7 February 1991), and the Air Force Health Study 1992 Followup Examination Results (2 May 1995).

Given the relationship of the 1997 follow-up to the previous studies, portions of these documents have been reproduced or paraphrased in this report. In addition, portions of the Air Force Health Study Statistical Plan for the 1997 follow-up (20 May 1998) have been used in the development of this report. The purpose of this notice is to acknowledge the authors of these previous study reports and documents.

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22 February 2000

Volume I

1997 Follow-up Examination Results

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TABLE OF CONTENTS

VOLUME I

List of Tables

List of Figures

TABLE OF CONTENTS-REPORT

EXECUTIVE SUMMARY

1997 FOLLOW-UP EXAMINATION REPORT

The Air Force Health Study (AFHS) is an epidemiological investigation to determine whether adverse health effects exist in Air Force personnel who served in Operation Ranch Hand units in Vietnam from 1962 to 1971, and whether these adverse health effects can be attributed to occupational exposure to Herbicide Orange (or its dioxin contaminant). A comparison group was formed from Air Force veterans who flew or maintained C-130 aircraft in Southeast Asia (SEA) during the same time period as those who served in the Ranch Hand units and who were not involved with spraying herbicides. The baseline study was conducted in 1982; follow-up studies were performed in 1985, 1987, 1992, and 1997. Participation was voluntary, and consent forms were signed by the participant at the examination site. An additional evaluation is planned for 2002. This report presents the results from the statistical analyses of the data from the 1997 follow-up examination.

In the baseline study, each living Ranch Hand was matched with a randomly selected Comparison based on age, race, and military occupation. At each follow-up study, noncompliant Comparisons were replaced from the set of living Comparisons, matched by age, race, military occupation, and self-perception of health. A total of 2,121 veterans participated in the 1997 follow-up examination. Of the 1,101 eligible Ranch Hands, 870 (79.0%) participated in the 1997 follow-up examination. A total of 839 of the 1,151 eligible Original Comparisons (72.9%) participated. Of the 768 eligible Replacement Comparisons, 412 (53.6%) chose to attend the examination. A total of 1,251 Comparisons attended the 1997 follow-up examination. Eighty-six percent (819 of 949) of living Ranch Hands and 87 percent of living Comparisons (976 of 1,116) who were fully compliant at the baseline examination returned for the 1997 follow-up examination.

This report presents conclusions drawn from the statistical analyses of 266 health-related endpoints in 10 clinical areas: general health, neoplasia, neurology, psychology, gastrointestinal, cardiovascular, hematology, endocrine, immunology, and pulmonary. Analysis was not performed on nine of these endpoints because of a sparse number of abnormalities. Data were collected from a medical records review, previous examinations, and the physical and laboratory examinations and questionnaire administered at the 1997 follow-up examination. The analyses focused on group differences between the exposed (Ranch Hand) and unexposed (Comparison) cohorts, as well as on the association between serum dioxin levels and each health-related endpoint among the Ranch Hands.

Four statistical models were used to evaluate the relation between the health status of study participants and their herbicide or dioxin exposure. The first model (Model 1) examines contrasts between Ranch Hands and Comparisons using group as a proxy for herbicide exposure and does not incorporate serum dioxin measurements. However, it is assumed in this model that all Ranch Hands were exposed and all Comparisons were not exposed to herbicides. Each of the following three models incorporates estimates of serum dioxin in either initial or current form. Current serum dioxin was based on measurements from the 1987 examination. When a 1987 dioxin measurement was not available, measurements from the 1992 or 1997 examinations were used to supplement the 1987 measurement. Initial serum dioxin was extrapolated from the current serum dioxin measurement to time of duty in SEA. The second model (Model 2) examines estimated initial serum dioxin levels, extrapolated from current serum dioxin measurements and assuming first-order kinetics and a constant dioxin elimination rate. The third model (Model 3) categorizes the Ranch Hand cohort according to serum dioxin levels and contrasts each Ranch Hand category with the Comparisons having background serum dioxin levels. The fourth model (Model 4) uses a 1987 lipid-adjusted measure of serum dioxin. This model requires no assumptions about serum dioxin elimination.

The extrapolated initial dose and lipid-adjusted dioxin measurements in Models 2, 3, and 4 may not be good measures of exposure if elimination rates differ among individuals.

In the general health assessment, the self-perception of health analysis revealed significant differences between Ranch Hands and Comparisons, with more Ranch Hands than Comparisons indicating their health as fair or poor. As in previous examinations, the difference was most apparent in enlisted groundcrew, who had the highest average dioxin levels. This observation also was confirmed in the categorized dioxin analysis, where Ranch Hands with the highest dioxin levels perceived their health as fair or poor more often than Comparisons. Also, among Ranch Hands, those with the higher 1987 dioxin levels reported fair or poor health more often than Ranch Hands with lower levels. These results were consistent with the 1985, 1987, and 1992 examinations. No group differences were noted in the appearance of illness or relative age, as recorded by examining physicians, nor were these variables correlated with serum dioxin levels in the Ranch Hand cohort. The analysis of body fat indicated positive associations with dioxin levels. The results of the 1997 examination confirmed those of the 1992 examination and appear consistent with a difference in dioxin pharmacokinetics in obese versus lean individuals. No differences in either the risk of an abnormal erythrocyte sedimentation rate between Ranch Hands and Comparisons or the relations between abnormal erythrocyte sedimentation rates and dioxin levels were observed during the 1997 examination. Erythrocyte sedimentation rates increased as 1987 dioxin levels increased. Longitudinal analyses showed that Ranch Hands, particularly the enlisted personnel, had a greater percentage of abnormal erythrocyte sedimentation rates than did Comparisons during the 15 years of the study since 1982. These analyses also showed that the percentages of abnormalities increased from 1982 to 1997 as dioxin levels increased. This result was seen at the 1987 study, but not in 1992. This positive association raises the possibility of a subtle inflammatory, infectious, or occult malignant disease process related to the body burden of dioxin. In conclusion, fair or poor self-perception of health displayed an adverse association with dioxin. Increased body fat was associated with increased levels of dioxin, a finding most likely related to the pharmacokinetics of dioxin. Longitudinal analyses indicated an increased risk of abnormal erythrocyte sedimentation rates in Ranch Hands over Comparisons in the 15 years of the AFHS, and a relation between abnormal erythrocyte sedimentation rates and levels of dioxin during these 15 years. Other measures of general health revealed no association with levels of dioxin.

In the assessment of malignant neoplastic disease, at the end of 15 years of surveillance, Ranch Hands as a group exhibited a nonsignificant increase in the risk of malignant neoplastic disease relative to Comparisons (relative risk=1.06, 95% confidence interval: [0.80,1.41]). Military occupation contrasts were inconsistent and, therefore, not supportive of an adverse effect of herbicide or dioxin exposure on the occurrence of malignancies. Ranch Hand enlisted groundcrew, the occupation with the highest dioxin levels and, presumably, the highest herbicide exposure, exhibited a decreased prevalence (relative risk=0.78, 95% confidence interval: [0.51,1.19]). Enlisted flyers (relative risk=1.63, 95% confidence interval: [0.91,2.92]) and officers (relative risk=1.14, 95% confidence interval: [0.79,1.65]), occupations with lower dioxin levels, exhibited nonsignificant increases in the prevalence of malignant disease. The risk of malignant disease was nonsignificantly increased among Ranch Hands having the highest dioxin levels (relative risk=1.01, 95% confidence interval: [0.66,1.57]). Longitudinal analyses found no significant group differences with regard to the risk of malignancy and no pattern suggestive of an adverse relation between herbicide or dioxin exposure and the occurrence of malignant neoplastic disease.

In the neurological assessment, four neurological disorders and extensive physical examination data on cranial nerve function, peripheral nerve status, and central nervous system coordination processes were analyzed. Inflammatory diseases, as verified by a medical records review, were increased in Ranch Hands relative to Comparisons in terms of both a group designation and categorized dioxin levels. Peripheral disorders, as verified by a medical records review, increased in Ranch Hands as levels of 1987 dioxin increased. Neck range of motion abnormalities were increased in Ranch Hands relative to Comparisons in

terms of both a group designation and categorized dioxin levels. The increase in abnormalities for Ranch Hands relative to Comparisons was noted in enlisted flyers. An increase in the risk of an abnormal muscle status was observed in Ranch Hand enlisted groundcrew. A significant association between initial dioxin and abnormalities of both visual fields and the patellar reflex was observed. Indices of polyneuropathy showed an increase in the prevalence of abnormality in Ranch Hands relative to Comparisons and a positive association with initial dioxin, categorized dioxin, and 1987 dioxin levels. In summary, although a common etiology in these findings is not apparent, a statistically significant increase in neurological disease appears in Ranch Hands historically, on physical examination, and as reflected in several of the composite polyneuropathy indices. Further, the associations of abnormal neck range of motion with categorized dioxin and a history of peripheral disorders with 1987 dioxin provide evidence of an association of neurological disease with elevated dioxin levels. The results of the analysis of the polyneuropathy indices also provide support of a statistical association between elevated dioxin levels and neurological disease; however, the clinical importance of this finding is uncertain.

Five psychological disorders, which were verified by a medical records review, and 12 measures from the Symptom Checklist-90-Revised (SCL-90-R) inventory were examined in the psychology assessment. The SCL-90-R consisted of nine primary symptom dimensions and three broad indices of psychological distress. In enlisted groundcrew a significantly greater percentage of Ranch Hands than Comparisons had a history of other neuroses. All other significant results from analyses of Ranch Hands versus Comparisons showed a greater percentage of Comparisons than Ranch Hands with high SCL-90-R scores. Associations between initial dioxin and the psychological endpoints were either nonsignificant or revealed a significant decrease in high SCL-90-R scores as initial dioxin increased. Differences in the history of psychological disorders and the prevalence of high SCL-90-R scores were examined between Comparisons and Ranch Hands categorized by dioxin levels. Ranch Hands in the low dioxin category and the low plus high dioxin category displayed a significantly higher occurrence of other neuroses than did Comparisons. The relation between the 1987 dioxin levels and the psychological endpoints was examined and all results were nonsignificant. In summary, Ranch Hand veterans exhibited a significantly increased prevalence of other neuroses among enlisted groundcrew, the military occupation with the highest dioxin levels and, presumably, the greatest herbicide exposure. Consistent increases in the prevalence of other neuroses with dioxin levels were found. No consistent relation was found between any SCL-90-R score and any measure of herbicide or dioxin exposure. The relation between other neuroses and herbicide exposure and dioxin levels will be described in greater detail in a separate report.

The gastrointestinal assessment was based on eight disorders as determined from a review and verification of each participant's medical records, a physical examination determination of hepatomegaly, and 29 laboratory measurements or indices. The laboratory parameters included measurements of hepatic enzyme activity, hepatobiliary function, lipid and carbohydrate indices, and a protein profile. In addition, the presence of hepatitis and fecal occult blood was investigated. Analyses of Ranch Hands versus Comparisons showed higher mean levels of alkaline phosphatase, α-1-antitrypsin, and haptoglobin in Ranch Hands than in Comparisons. In addition, significantly more Ranch Hands than Comparisons had high haptoglobin levels. A review of medical records showed a positive association between initial dioxin and other liver disorders. The other liver disorders condition consisted primarily of nonspecific laboratory test elevations. A significant association between initial dioxin and high levels of aspartate aminotransferase (AST) also was revealed. Analyses of categorized dioxin revealed a significantly higher percentage of other liver disorders among Ranch Hands in the high dioxin category than among Comparisons. Higher mean levels of gamma glutamyl transferase (GGT), triglycerides, and α-1-antitrypsin were observed in Ranch Hands in the high dioxin category than in Comparisons. Ranch Hands in the high dioxin category had a greater prevalence of abnormal AST, triglyceride, and prealbumin levels than did Comparisons. Many significant associations between the laboratory examination variables and 1987 dioxin levels were observed. In both the continuous and discrete forms, the hepatic enzymes alanine

aminotransferase (ALT), AST, and GGT revealed significant, positive associations with 1987 dioxin. In addition, significant positive associations between 1987 dioxin and the ratio of cholesterol to high-density lipoprotein (HDL), triglycerides, and creatine phosphokinase were present. In summary, the analysis of the 1997 follow-up data reflected patterns that have been observed and documented in prior examinations. Isolated group differences exist, but 1987 dioxin levels are strongly related to hepatic enzymes such as AST, ALT, and GGT, and to lipid-related health indices such as cholesterol, HDL, and triglycerides. These results are consistent with a dose-response effect and may be related to unknown subclinical effects of dioxin. Although hepatic enzymes and lipid-related indices showed an association with dioxin, there was no evidence of an increase in overt liver disease.

In the cardiovascular assessment, analyses revealed that Ranch Hands had a significantly higher percentage of participants with a history of heart disease (excluding essential hypertension) than Comparisons and in particular, among enlisted flyers. However, the risk of disease was not significantly increased in Ranch Hand enlisted groundcrew, the military occupation with the highest dioxin levels. The association between heart disease and initial dioxin showed a negative dose-response trend, with heart disease decreasing as initial dioxin increased. Furthermore, Ranch Hands in the background and low dioxin categories had more heart disease than did Comparisons, but this increase was not seen in Ranch Hands in the high dioxin category. Increases in tachycardia and other electrocardiograph (ECG) findings, such as pre-excitation, were seen for Ranch Hands in the high dioxin category, although the analyses were based on a small number of abnormalities. A significant positive association between initial dioxin and evidence of prior myocardial infarction from the ECG was observed in Ranch Hands, and a marginally significant positive association was observed between 1987 dioxin and evidence of prior myocardial infarction from the ECG. A positive association between 1987 dioxin and a history of essential hypertension also was observed in Ranch Hands. In contrast to previous AFHS examinations, no relation was found between peripheral pulse abnormalities and any measure of exposure. In summary the current study has documented that Ranch Hands are more likely than Comparisons to have historical evidence for heart disease (excluding essential hypertension) but are no longer at greater risk for the occurrence of pulse deficits. By all other indices, the prevalence of cardiovascular disease appears similar in both cohorts. For the first time, there is evidence that levels of dioxin may be a risk factor for the development of essential hypertension and prior myocardial infarction as indicated by interpretation of the ECG. As of 1997, the verified history of essential hypertension was associated with 1987 dioxin, and the evidence of prior myocardial infarction from the ECG was associated with initial dioxin. These findings, in conjunction with the increase in the number of deaths caused by diseases of the circulatory system for Ranch Hand nonflying enlisted personnel based on the 1994 AFHS mortality update, showed associations that require further study. A biological mechanism for the relation among dioxin levels and heart disease is unknown.

In the hematologic assessment, five cell count measures, six measures of absolute blood counts, a coagulation measure, and red blood cell morphology were analyzed. In the analyses of these variables, only platelet count exhibited significant dose-response associations with the levels of dioxin. Among enlisted personnel, Ranch Hands exhibited significantly higher mean platelet counts than did Comparisons. Ranch Hands in the high dioxin category also exhibited a significantly higher mean platelet count than did Comparisons. The mean differences were small and, therefore, the clinical importance of these findings is unknown. The results in the 1997 follow-up study parallel the findings of the 1987 and 1992 follow-up studies. In conclusion, apart from platelet count, there appears to be little evidence to support a relation between prior dioxin exposure and hematopoietic toxicity.

The assessment of the endocrine system yielded an extensive evaluation of thyroid, pancreatic, and gonadal function and their relation to dioxin exposure. A significantly increased risk of abnormally high thyroid stimulating hormone values was found in Ranch Hand enlisted groundcrew. A positive association between diabetes and initial and 1987 dioxin was observed. Consistent with previous reports, the prevalence of

diabetes among Ranch Hands with high dioxin levels was significantly increased. A greater percentage of Ranch Hands than Comparisons used insulin to control their type 2 diabetes, primarily among officers and enlisted groundcrew. The percentage of Ranch Hands requiring insulin to control their type 2 diabetes increased with initial dioxin. A greater percentage of Ranch Hands in the high dioxin category required insulin to control their type 2 diabetes than did Comparisons. The percentage of Ranch Hands who treated their diabetes through diet only and the percentage who used oral hypoglycemics increased with 1987 dioxin level. The time to diabetes onset was significantly shorter for Ranch Hands with higher initial dioxin and 1987 levels. Both fasting glucose and α-1-C hemoglobin increased as initial dioxin and 1987 dioxin increased. Increased mean α-1-C hemoglobin levels also were observed for Ranch Hands with high dioxin levels. The presence of fasting urinary glucose also increased with 1987 dioxin. Although cause and effect have not been established, the results cited above provide further evidence for an association between glucose intolerance and levels of dioxin.

The immunologic assessment was based on laboratory data on six lymphocyte cell surface markers, absolute lymphocyte counts, three quantitative immunoglobulins, and six measurements from an autoantibody panel. The six cell marker measurements were carried out on a random sample of approximately 40 percent of the participants because of the complexity of the assay and the expense of the tests. Group analyses revealed significant findings for the analyses of CD16+56+ cell (natural killer cell) counts and for the mouse stomach kidney (MSK) smooth muscle antibody test in enlisted flyers. Among enlisted flyers, the mean CD16+56+ cell count was greater for Comparisons than for Ranch Hands, and a greater percentage of Comparisons than Ranch Hands had a smooth muscle antibody present. Negative smooth muscle and mitochondrial antibody tests are considered to be normal. For these analyses, the magnitude of the mean differences was small and, therefore, the clinical importance of these findings is unknown. Consistent with the previous two physical examinations, IgA increased significantly with initial dioxin, but was not significantly increased in enlisted groundcrew or the high dioxin category, and IgA did not increase significantly with 1987 dioxin. The IgA results, although significant, were small in magnitude and their clinical importance is unknown. When comparing categorized dioxin levels between Ranch Hands and Comparisons, a significantly higher CD16+56+ cell count mean was observed among Comparisons than among Ranch Hands in the high dioxin category. Analyses revealed significant associations between 1987 dioxin levels and CD3+ cell (T cell) count, CD4+ cell (helper T cell) count, and CD3+CD4+ cell (helper T cell) count. The cell counts increased as 1987 dioxin increased. In summary, these findings and the findings from past examinations do not provide evidence of a biologically meaningful dose-response effect for body burden of dioxin on parameters of immunologic assessment. The statistically significant relations suggest the need for continued evaluation.

To assess pulmonary status, verified histories of asthma, bronchitis, and pneumonia were studied. A composite measure of thorax and lung abnormalities, as determined from the presence of asymmetrical expansion, hyperresonance, dullness, wheezes, rales, chronic obstructive pulmonary diseases, or the physician's assessment of abnormality, also was analyzed. A routine chest x ray and five measures of pulmonary function using standard spirometric techniques were analyzed. Few significant increases in adverse pulmonary conditions were observed for Ranch Hands, and isolated and inconsistent associations between the pulmonary endpoints and dioxin were seen. No consistent pattern or dose-response relation was evident. Ranch Hands in the background dioxin category exhibited a significantly higher percentage of abnormalities on the chest x ray than did Comparisons. Ranch Hand officers had a significantly higher prevalence of mild obstructive abnormality than did Comparison officers; the corresponding contrast was not significant in 1992, and officers were not analyzed as a separate stratum in 1982, 1985 or 1987. The relation between mild obstructive abnormality in Ranch Hand officers and other indicators of herbicide exposure, such as job (pilot, navigator, nonflyer), the number of missions flown, the percentage of missions that were herbicide missions, and reported drinking of herbicide (yes, no) will be summarized in a separate report. In summary, analysis of historical, physical examination, and laboratory data revealed no

consistent relation between herbicide exposure or dioxin levels and pulmonary disease. The prevalence of mild obstructive abnormalities was significantly increased in Ranch Hand officers. The meaning of this finding is unclear because the risk was not significantly increased in Ranch Hand enlisted groundcrew—the military occupation with the highest dioxin levels.

Certain facts should be considered when drawing conclusions from the statistical analysis of the 1997 follow-up examination results. First, the Ranch Hand and Comparison veterans were not blinded to group membership. In addition, there are often difficulties associated with multiple testing. With repeated statistical testing, the likelihood of a test indicating some artifactual association is high. But longitudinal comparisons of previous examinations may show a consistent association, supporting a non-artifactual relation. Longitudinal tests, however, of the same population clearly are not independent tests. If a chance association was present at the first physical examination, it would tend to persist in subsequent examinations. Conversely, depending on site and mode of action, the association would be expected to increase with time (if latency or other chronic effects predominate) or decrease with time (if the current dioxin level predominates in the mechanism). It is also important to note that some conditions do not appear with reasonable frequency until middle age or later. Therefore, in the early years of the study an increased relative risk might have been masked by abnormalities too sparse for meaningful analysis.

The report recognizes two major limitations to the study. First, the results cannot be generalized to other groups (such as all Vietnam veterans or Vietnamese civilians) who have been exposed in different ways and to different levels of herbicide. We do not know what effect herbicides or dioxin have at levels other than those found in our study group, or from other sources such as contaminated food. Groups with higher exposures may well have effects not seen in our study. Second, the size of the study makes it difficult to detect increases in rare diseases, so small increases of these diseases may be missed by the study. For example, since liver cancer is very rare, even a tenfold increase may not be detected.

The site and mode of action of dioxin in the body could itself either cause or obscure a relation. Receptors might be activated only after a certain dioxin threshold value had been exceeded—that is, a value exceeding the body's capability to safely store dioxin. If, on the other hand, dioxin caused a competitive inhibition of receptor actions normally stimulated by other substances, there might be a "no-threshold" effect. Depending on the nature (lipid or non-lipid) and type of function of the hypothetical receptor site, an increase in body fat over time might either cause an increase in dioxin effect because of a greater volume of distribution or a decrease in dioxin effect because of a lesser concentration at the receptor site.

Strength of association is also an issue in a study of a population this size. A study with a population of 2,121 lacks power to determine increases in relative risks for rare events (such as soft tissue sarcoma) because such events are unlikely to occur in large numbers in a group this small. While certain occupational toxins have a clear diagnostic pathology (e.g., mesothelioma for asbestos, hepatic angiosarcoma for vinyl chloride) virtually nonexistent in the absence of the toxin, other toxins merely increase the risk of nondiagnostic pathology. For example, this study would likely not discern an increase in the relative risk for a rare tumor that does not have a clear diagnostic pathology. By assessing the pathology observed in association with other known environmental risk factors (e.g., tobacco use, alcohol use) it is sometimes possible to provide a limit in the magnitude of effect missed; however, this study has inherent bounds in detecting modest increases in relative risk for infrequent pathology.

A final difficulty is the presence of a true association that is noncausal. An example might be a condition not caused by dioxin, but resulting in or from an altered dioxin half-life. In this case, a correlation might be high in the total absence of causality.

Clearly, there are many issues to be considered in interpreting these results. With these issues in mind, certain assessments were made by looking at a number of factors. Among these factors are longitudinal trends, biological plausibility, consistency with animal toxicology, the presence of a dose-response relation, and strength of association. But, meeting all of these criteria would not guarantee causality, nor would failing these criteria guarantee the lack of an effect. It can be argued, however, that the good faith application of these particular methods should be the starting point for generating hypotheses for experimental examination through in vitro and in vivo testing, as well as through further epidemiological analysis of these and other exposed groups.

Based on the findings of the 1997 examination, and subject to the qualifications considered above, the study investigators have drawn the following conclusions.

1. **Diabetes:** Consistent with previously reported results, current data indicate a significant and potentially meaningful adverse relation between serum dioxin levels and diabetes. A significant dose-response was found, with Ranch Hands in the high dioxin category exhibiting an increase in disease prevalence (relative risk=1.47, 95% confidence interval: [1.00,2.17]). The finding is supported by a dioxin-related increase in disease severity, a decrease in the time from exposure to first diagnosis, and an increase in fasting glucose and α-1-C hemoglobin. Similar patterns were observed in 1987 and 1992.

2. **Cardiovascular Abnormalities:** Cardiovascular findings are mixed, but, in context with the increased cardiovascular mortality in nonflying enlisted Ranch Hands, are suggestive of an adverse effect of herbicide and dioxin exposure. As a group, Ranch Hands have experienced a statistically significant increase in the prevalence of heart disease (excluding essential hypertension) (relative risk=1.26, 95% confidence interval: [1.05,1.51]). The increase was more than doubled among enlisted flyers (relative risk=2.10, 95% confidence interval: [1.27,3.28]), but not significantly increased among enlisted groundcrew (relative risk=1.10, 95% confidence interval: [0.84,1.42])—the military occupation with the highest dioxin levels. The prevalence of diagnosed essential hypertension and the percentage of Ranch Hands with ECG findings of prior myocardial infarction increased significantly with initial dioxin. Peripheral pulse abnormalities increased with dioxin levels in 1987 and 1992, but did not increase with dioxin levels in 1997. These findings, together with increased cardiovascular mortality in Ranch Hand nonflying enlisted personnel, suggest that herbicide or dioxin exposure may be related to cardiovascular abnormalities.

3. **Peripheral Polyneuropathy:** Although a common etiology is not apparent, a statistically significant increase in neurological disease appears in Ranch Hands historically, on physical examination, and as reflected in several of the composite polyneuropathy indices. Peripheral disorders, as verified by a medical records review, increased in Ranch Hands as levels of 1987 dioxin increased. Indices of bilateral peripheral polyneuropathy, confirmed by vibrotactile measurements in the feet, significantly increased with initial dioxin level, were significantly increased in the high dioxin category, and significantly increased with 1987 dioxin. These findings are new and appear consistent with polyneuropathies observed in studies of industrial exposure; however, the numbers of affected veterans are small and the clinical importance of the findings are uncertain.

4. **Serum Lipid Abnormalities:** There were consistent and significant increases in cholesterol, triglycerides, and the cholesterol-HDL ratio with initial and 1987 dioxin. HDL decreased significantly as dioxin increased. These findings also were observed in 1987 and 1992.

5. **Liver Enzymes:** Analysis of liver function reflected patterns that have been observed in prior examinations. Isolated group differences existed, but 1987 dioxin levels were strongly related to increases in hepatic enzymes such as AST, ALT, and GGT and, as previously noted, cholesterol, triglycerides, and HDL. These results were consistent with an adverse dose-response and may be related to subclinical effects of unknown importance. Although hepatic enzymes increased with dioxin, there is no evidence of a corresponding increase in overt liver disease.

6. **Malignant Neoplastic Disease:** At the end of 15 years of surveillance, Ranch Hands as a group exhibited a nonsignificant increase in the risk of malignant neoplastic disease relative to Comparisons (relative risk=1.06, 95% confidence interval: [0.80,1.41]). Military occupation contrasts were inconsistent and, therefore, not supportive of an adverse effect of herbicide or dioxin exposure on the occurrence of malignancies. Ranch Hand enlisted groundcrew, the occupation with the highest dioxin levels and, presumably, the highest herbicide exposure, exhibited a decreased prevalence (relative risk=0.78, 95% confidence interval: [0.51,1.19]). Enlisted flyers (relative risk=1.63, 95% confidence interval: [0.91,2.92]) and officers (relative risk=1.14, 95% confidence interval: [0.79,1.65]), occupations with lower dioxin levels, exhibited nonsignificant increases in the prevalence of malignant disease. The risk of malignant disease was nonsignificantly increased among Ranch Hands having the highest dioxin levels (relative risk=1.01, 95% confidence interval: [0.66,1.57]). Longitudinal analyses found no significant group differences with regard to the risk of malignancy and no pattern suggestive of an adverse relation between herbicide or dioxin exposure and the occurrence of malignant neoplastic disease.

In conclusion, diabetes and cardiovascular abnormalities represent the most important dioxin-related health problems seen in the AFHS. These two areas appear to have the greatest magnitude of effect in terms of quality of life and healthcare costs. Clearly, there are biological interrelations among both of these outcomes that make interpretations difficult. From a public health perspective, these two areas demand the greatest attention.

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Table of Contents

List of Tables

1 INTRODUCTION

This chapter describes the purpose and background of the Air Force Health Study (AFHS), and provides an overview of the study design, morbidity component, and format of this report. In addition, it provides considerations that should be made when interpreting the results provided in this report.

1.1 PURPOSE OF THE REPORT

The subject of this report is the 1997 morbidity follow-up study of the AFHS. The objective of the morbidity follow-up is to continue the investigation of the possible long-term health effects following exposure to herbicides with specific emphasis on Herbicide Orange containing 2,4-D, 2,4,5-T, and 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) or dioxin. The principal investigators and the AFHS reports have focused on TCDD. This focus has been the direction for most of the study as derived from the early peer review groups, review of the literature, and the Advisory Committee. However, Model 1, the Ranch Hand versus Comparison contrast, does address in a general way the exposure to picloram and cacodylic acid. In addition, dioxin is a biomarker that the study has used as a surrogate to estimate exposure to phenoxy herbicides, described in greater detail in Section 1.6.2 of this chapter. This report describes the procedures and results of this follow-up study. It was written primarily for epidemiologists, clinicians, and biostatisticians. Familiarity with the Study Protocol and prior mortality and morbidity reports is essential to a full understanding of this 20-year study. This report format has been established to be similar to previous reports so that readers can compare results across study cycles. All statistical analyses in this report were prescribed by the Air Force prior to data collection. This report, prepared by Science Applications International Corporation (SAIC), is submitted as partial fulfillment of Air Force Contract No. F41624-96-C-1012.

1.2 BACKGROUND

In January 1962, President John F. Kennedy approved a program of aerial herbicide dissemination for the purpose of defoliation and crop destruction, in support of tactical military operations in the Republic of Vietnam (RVN). This program, code-named Operation Ranch Hand, dispersed approximately 19 million gallons of herbicides on an estimated 10 to 20 percent of South Vietnam from 1962 to 1971. The herbicides sprayed were code named Herbicide Green, Herbicide Pink, Herbicide Purple, Herbicide Orange, Herbicide White, and Herbicide Blue. 2,4,5-T was an active ingredient in Green, Pink, Purple, and Orange, and TCDD was produced as an inadvertent contaminant of 2,4,5-T during the manufacturing process. 2,4-D was an active ingredient in Purple, Orange, and White. Picloram was an active ingredient in White; cacodylic acid was the active ingredient in Blue. Of the 19 million gallons of herbicide dispersed, approximately 11 million gallons were Herbicide Orange, also called Agent Orange, the primary defoliant of the six herbicides used in the program (1, 2).

From the start, Operation Ranch Hand was heavily scrutinized because of the controversial nature of the program and the political sensitivity to charges of chemical warfare contained in enemy propaganda. The concerns were initially based on military, political, and ecological issues, but shifted to issues of health in 1970. The primary concern in the controversy over the human health effects of these herbicides was related to the dioxin impurity created as a byproduct in the manufacturing process of 2,4,5-T, a component in four of the six herbicides released. The Air Force estimates that 368 pounds of dioxin were released over 6 million acres in South Vietnam (1). Claims of exposure to herbicides, particularly to Herbicide Orange, and perceived adverse health effects among U.S. military service personnel resulted

in substantial controversy and, eventually, a class action litigation. Social concern for the Herbicide Orange issue continues to be reflected in scientific research, media presentations, congressional hearings, and legal action.

Since 1970, governmental agencies, universities, and industrial firms have funded numerous human and animal studies of dioxin effects. A key scientific issue in these studies was the extent of exposure (e.g., who was exposed and to what extent each individual was exposed). Unfortunately, in many of the human studies, population identification and exposure estimation have been scientifically elusive.

In October 1978, the Air Force Deputy Surgeon General made a commitment to Congress and the White House to conduct a health study on the Operation Ranch Hand population. This population comprised the aviators and ground support crews who disseminated the majority of the defoliants in the RVN. The Surgeon General tasked the U.S. Air Force School of Aerospace Medicine at Brooks Air Force Base, Texas, to develop a study protocol. In 1982, after extensive peer review, the epidemiological study began and the Study Protocol was published (3). The Brooks Air Force Base organizations responsible for executing the protocol have been reorganized and renamed several times from 1982 to the present. Currently, the Air Force Research Laboratory, Human Effectiveness Directorate, is responsible for the technical aspects of the study, and the Aeronautical Systems Center, Human Systems Program Office, is responsible for program management.

Studies of serum dioxin levels have suggested that of all the military personnel who served in the RVN, the Ranch Hand cohort was one of the most highly exposed to herbicides. In 1987, when the serum assay became available, the Air Force initiated a collaborative study with the Centers for Disease Control and Prevention (CDC) to measure the serum dioxin levels in the AFHS population. The results of that study demonstrated that substantial elevated levels of dioxin could still be found in the serum of some Ranch Hands (4, 5). If dioxin caused an adverse health effect, then, based on the principle of dose-response, the Ranch Hands should have manifested more or earlier evidence of adverse health.

1.3 STUDY DESIGN

The purpose of the AFHS is to determine whether adverse health effects relative to a similar but unexposed group of Air Force veterans exist and can be attributed to occupational exposure to Herbicide Orange. The study, consisting of mortality, morbidity, and reproductive outcome components, is based on a matched cohort design in a nonconcurrent prospective setting with follow-up studies. A baseline morbidity study and five follow-up morbidity studies over 20 years provide a comprehensive approach to the detection of adverse health effects. Complete details on the design are provided in the Study Protocol.

For the baseline study, the population ascertainment process identified 1,264 Ranch Hand personnel who served in the RVN between 1962 and 1971. At the beginning of the study, a Comparison group was identified consisting of veterans assigned to Air Force units operating C-130 cargo aircraft in Southeast Asia. A computerized selection procedure was used to identify Comparisons with similar characteristics to each Ranch Hand veteran. A maximum of 10 Comparisons for each Ranch Hand was selected, matching on age, race, and military occupation (officer-pilot; officer-navigator; officer-other; enlisted flyer; enlisted groundcrew). After personnel records review, an average of eight Comparison subjects were matched to each Ranch Hand.

A replacement strategy was devised to maintain participation of the Comparisons. Noncompliant Comparisons were to be replaced by Comparisons with the same values of the matching variables (age, race, and military occupation at the baseline examination) and the same health perception. In this way,

the Replacement Comparisons would serve as surrogates for Comparisons who refused to participate. Complete information on the selection and participation of study subjects can be found in Chapter 5, Study Selection and Participation.

The mortality component addresses mortality from the time of the RVN assignment. A baseline mortality study was conducted in 1982, and the mortality follow-up study consists of annual mortality updates for 20 years. For the baseline mortality study and the first four updates, five individuals were randomly selected from the matched Comparison set for each Ranch Hand for a 1:5 design. After 1987, the design was expanded to include all 19,080 veterans in the Comparison population.

1.4 MORBIDITY COMPONENT

The baseline morbidity component, begun in 1982, reconstructed the medical history of each participant by reviewing and coding past medical records. A cross-sectional element, designed to assess the participant's current state of physical and mental health, was based on comprehensive physical examinations and questionnaires. For the morbidity component of the study, each living Ranch Hand and a random living member of his Comparison set were selected to participate in the examination. The morbidity study follow-up comprises sequential questionnaires, medical records review, and physical examinations in 1985, 1987, 1992, 1997, and 2002. Participation was voluntary and each participant signed an informed consent form at the examination site. Previous study results are summarized in each clinical chapter.

The baseline morbidity assessment, conducted in 1982, disclosed few differences between the Ranch Hands and Comparisons (6). The sustained commitment to pursue the Herbicide Orange question to its scientific conclusion was demonstrated by the conduct of the first two morbidity follow-up studies in 1985 and 1987. These examinations provided the opportunity to confirm or refute some of the baseline findings and to explore subtle longitudinal changes. In the follow-up examinations, the physical and mental health status of the participants during the time interval since the baseline study was assessed. The results of the follow-up studies showed a subtle but consistent narrowing of medical differences between the Ranch Hands and Comparisons since the baseline study in 1982. There was not sufficient evidence to implicate a relation between herbicide exposure and adverse health in the Ranch Hand group.

For the baseline study and the 1985 and 1987 follow-up studies, the major focus of the analyses was to compare the health status of the Ranch Hands (i.e., the exposed cohort) with that of the Comparisons (i.e., the unexposed cohort). Methodology to measure dioxin body burden in blood was not made available until February 1987. During the 1987 physical examination, the Air Force initiated a collaborative study with CDC to measure dioxin levels in the serum of Ranch Hands and Comparisons (4, 7, 8). The measurement of serum dioxin levels led to a statistical evaluation to assess dose-response relations between dioxin and the approximately 300 health-related endpoints in 12 clinical areas. This was the first large-scale study of dose-response effects based on a direct measurement of current dioxin. The statistical analyses associated with the serum data evaluated the association between a specified health endpoint and dioxin among the Ranch Hands. The analyses also contrasted the health of various categories of Ranch Hands having differing serum dioxin levels with the health of Comparisons having background levels (10 parts per trillion (ppt) or less) of serum dioxin (9). The analysis of dose-response relations based on serum assays provided an important enhancement from the previous AFHS investigations.

In 1992, the fourth examination was initiated. During a 2½-year period, data for 12 clinical areas were collected and analyzed. As in previous reports, the analysis focused on group differences between the Ranch Hand and Comparison cohorts, as well as on the association of each health-related endpoint with

extrapolated initial and current serum dioxin levels. Findings revealed a consistent relation between dioxin and body fat that was initially noted in the analysis of the 1987 examination results. Cholesterol and the cholesterol-to-HDL ratio were found to be associated with current serum dioxin levels (10). Evidence for a possible association between glucose intolerance, impaired insulin production, and dioxin levels was revealed. Also revealed was a significant association between selected peripheral pulse abnormalities and dioxin levels, and a significant decrement in self-perceived health status of Ranch Hands. Other health endpoints revealed no consistent patterns within or across clinical areas that were suggestive of an adverse relation between health and herbicide or dioxin exposure.

The fifth examination began in 1997. As in 1985, 1987, and 1992, this study was conducted by SAIC in conjunction with Scripps Clinic and National Opinion Research Center (NORC). Analysis of data collected at the 1997 study was the basis for this report. In a departure from previous AFHS reports, dermatologic and renal diseases, other than cancer, were not summarized in this report. Summaries of malignant skin conditions, as well as cancers of the genitourinary system and kidneys, were included in the neoplasia chapter. In past reports, the dermatologic assessment placed primary emphasis on six dermatologic disorders: comedones, acneiform lesions, acneiform scars, inclusion cysts, depigmentation, and hyperpigmentation. Secondary emphasis was given to a composite variable consisting of 16 other minor conditions (generally not associated with chloracne). No significant difference was found for any of these variables in the unadjusted analyses. The adjusted analyses closely mirrored the unadjusted analyses, with no significant difference noted between groups for any variable. Exposure index analyses supported dose-response relations for some of the variables in certain occupational strata, but did not reveal a strong pattern of results suggesting a relation between skin disease and herbicide exposure. In addition, a recently published analysis found no evidence of chloracne in Ranch Hand veterans and no detectable relation between dioxin and acne (11). While a dermatology examination was completed on each participant, because of these results in previous follow-up examinations, a statistical assessment of the data was not performed for the 1997 study.

Medical histories of renal disease and measures of renal function were collected at the 1997 AFHS physical examination; however, assessment of the renal data results was not included in this report for the following four reasons:

1. To our knowledge, there has been no evidence that the kidneys are target organs for dioxin toxicity.
2. The Institute of Medicine report on veterans and Agent Orange did not mention nonmalignant renal disease or renal function as a possible outcome of dioxin exposure (12).
3. No other epidemiological study has documented nonmalignant kidney disease or renal function as a target of dioxin toxicity.
4. All previous statistical analyses of renal disease and renal function have found no association with exposure group or with dioxin level.

Although the dermatology and renal data collected in the 1997 study were not analyzed for this report, they will be combined with the results from the 2002 physical examination and summarized in the final AFHS report.

1.5 ORGANIZATION OF THE REPORT

This report is organized as follows:

- Chapter 1 (Introduction) provides summary background information on the AFHS and discusses specific technical items and issues that may affect the different clinical area assessments.
- Chapter 2 (Dioxin Assay) describes the procedure used to draw blood for the serum dioxin measurements, the analytical method used to determine the dioxin level from the serum, and the quality control (QC) procedures associated with the serum dioxin data.
- Chapter 3 (Questionnaire Methodology) gives an overview of the development and implementation of the participant questionnaires.
- Chapter 4 (Physical Examination Methodology) describes the conduct and content of the physical examinations.
- Chapter 5 (Study Selection and Participation) presents the methods by which participants were selected and scheduled. This chapter also presents a discussion of the participant replacement strategy, the factors known or suspected to influence study participation, and sources of potential bias.
- Chapter 6 (Quality Control) provides an overview of the specific quality assurance and QC measures developed and used throughout the 1997 follow-up study.
- Chapter 7 (Statistical Methods) documents the statistical methods used in the individual clinical area assessments and the statistical procedures and results of the half-life analyses performed by the Air Force.
- Chapter 8 (Covariate Associations with Estimates of Dioxin Exposure) examines the associations between exposure (Ranch Hand, Comparison, and measures of dioxin exposure) and the individual covariates used in the different clinical assessments.
- Chapters 9 through 18 present the results and medical discussions of the statistical analyses of the dependent variables for each clinical area. Each chapter also contains a brief overview of pertinent scientific literature. The 10 clinical chapters are as follows:

  Chapter 9: General Health Assessment
  Chapter 10: Neoplasia Assessment
  Chapter 11: Neurological Assessment
  Chapter 12: Psychological Assessment
  Chapter 13: Gastrointestinal Assessment
  Chapter 14: Cardiovascular Assessment
  Chapter 15: Hematologic Assessment
  Chapter 16: Endocrine Assessment
  Chapter 17: Immunologic Assessment
  Chapter 18: Pulmonary Assessment

- Chapter 19 (Conclusions) summarizes the findings and medical discussions of the 10 clinical areas.
- Chapter 20 (Future Directions) summarizes the anticipated future activities and discusses possible modifications to the existing instruments and methodologies used to investigate the association between health status and dioxin exposure.

1.6 INTERPRETIVE CONSIDERATIONS

In interpreting results from any epidemiological study, no single result should be evaluated in isolation or at face value. Rather, interpretations should be addressed in the context of the overall study design, the data collection procedures, the data analysis methods, dose-response effects, strength of association, temporal relation, biological plausibility, and internal and external consistency. This especially applies to the AFHS. This effort is a large-scale, prospective observational study in which thousands of measurements are generated on each participant. Those measurements and diagnoses are subjected to extensive statistical analyses, testing thousands of individual hypotheses. Each positive result should be scrutinized relative to other findings in this and other studies, and relative to the statistical methods used and the medical and biological plausibility of the results. Conversely, the lack of a positive result only denotes that the hypothesis of no association was not rejected. This has a very different conclusion than the possibly incorrect assertion that there is no effect. In addition, no epidemiological study can establish that there is no effect; i.e., that dioxin is safe (13). Critical considerations in the evaluation of results from this study are reviewed below. Other interpretive considerations, such as adjustments to analyses for known confounders, multiple testing, trends in results within a clinical area, and power limitations, are discussed in greater detail in Chapter 7, Statistical Methods.

1.6.1 Study Design and Modeling Considerations

Biased results will be produced if the assumptions underlying any of the statistical models are violated. Four models were used in this report to analyze the health effects of herbicide exposure in Vietnam. The first model contrasts the exposed population (Ranch Hands) with an unexposed group (Comparisons). The second model evaluates the relation between estimated serum dioxin levels from the time of exposure (i.e., initial dioxin) with each health endpoint. The group contrast model is extended in the third model so that the Ranch Hand group is divided into three categories depending on 1987 levels and estimated initial levels of serum dioxin, and each category is contrasted with the Comparison group. The fourth model evaluates the association between the dependent variables and lipid-adjusted 1987 dioxin levels. The parameters of these four models are summarized in Table 1-1.

As in any epidemiological study, the group contrast (Ranch Hands versus Comparisons) is susceptible to bias toward the null hypothesis of no exposure effect, because of possible exposure misclassification. It may not be true that all Ranch Hands and no Comparisons were occupationally exposed. Recent dioxin data indicate that 44 percent of the Ranch Hands have only background serum dioxin levels. These Ranch Hands either were never exposed or their initially elevated serum dioxin levels may have decreased to background levels during the time period between exposure and serum dioxin measurement. The AFHS has no additional data with which to determine whether Ranch Hands currently having background dioxin levels had elevated levels in the past because there was no method of measuring dioxin in blood prior to 1987, and because no blood was collected and saved prior to 1982.

The model analyzing the association between health endpoints and extrapolated initial dioxin levels (Model 2) also is vulnerable to bias because it directly depends on two unvalidated assumptions: (a) that dioxin elimination is by first-order pharmacokinetics, and (b) that all Ranch Hands have the same dioxin half-life (8.7 years) (14). If dioxin elimination is first-order, but some Ranch Hands have a shorter half-life than others do, then there would have been misclassification of initial dioxin levels.

Table 1-1. Parameters of Exposure Assessment Models

Model	Cohort(s)	Subset of Cohort	Exposure Characterized by:	Covariates in Analysis (not including endpoint-specific covariates)
1	Ranch Hands and Comparisons	All participants	Group (Ranch Hands versus Comparisons and military occupation)	--
2	Ranch Hands	Lipid-adjusted 1987 dioxin measurement >10 ppt	Extrapolated initial dioxin	Body fat at time of blood measurement of dioxin
3	Ranch Hands and Comparisons	RH: 1987 dioxin measurement C: Lipid-adjusted dioxin measurement ≤10 ppt	Group (Ranch Hands versus Comparisons); Ranch Hands categorized according to 1987 dioxin and estimated initial dioxin levels	Body fat at time of blood measurement of dioxin
4	Ranch Hands	1987 dioxin measurement	Lipid-adjusted 1987 dioxin: (102.6*whole-weight 1987 dioxin/total lipids)	--

Note: RH = Ranch Hands.
C = Comparisons.

The half-life of dioxin has been found to change significantly with percent body fat in 213 Ranch Hand veterans with three dioxin measurements, derived from serum drawn in 1982, 1987, and 1992 (14). The half-life increased significantly with higher levels of obesity. The constant 8.7-year half-life used in this report was an estimate derived without adjustment for body fat (14). As a partial solution to the observed relation between half-life and obesity, analyses using dioxin or initial dioxin (Models 2 and 3) were adjusted for percent body fat at the time of the blood measurement of dioxin (see Chapter 7, Statistical Methods). A recent study of dioxin elimination in 20 men exposed during the Seveso accident has validated the first-order model (15), which was the basis for the half-life estimate used in this report; however, validated models of dioxin elimination adjusted for body fat or changes in body fat have not yet been derived.

To account for the possible misclassification of exposure between groups, the third statistical model categorizes Ranch Hands into three levels of exposure: background levels of lipid-adjusted dioxin, and low and high levels of estimated initial dioxin. Each Ranch Hand dioxin category is contrasted with Comparisons having background levels of lipid-adjusted dioxin. Although this model is less dependent upon the accuracy of the initial dioxin estimation procedure than the model using continuous initial dioxin estimates, the classification of the Ranch Hands is subject to bias if the half-life and first-order dioxin elimination assumptions are not true. Also, the Ranch Hands with background levels of lipid-adjusted serum dioxin may contain both unexposed Ranch Hands and exposed Ranch Hands whose serum dioxin levels have decreased to background levels. This will result in a bias toward the null hypothesis of no dioxin effect on the health endpoint.

The model that analyzes the association between a 1987 dioxin measurement and health endpoints (Model 4) may be less subject to bias than Models 1, 2, and 3; however, recent dioxin levels may not be a good measure of exposure if serum dioxin elimination rates differ among individuals. Serum dioxin levels were extrapolated from 1992 measurements to 1987 for Ranch Hand veterans without serum

dioxin levels measured in 1987. Serum dioxin levels also were extrapolated from 1997 measurements to 1987 for Ranch Hand veterans without levels measured in 1987 or 1992. These extrapolations were performed only if the most recent measurement was greater than 10 ppt. Therefore, these 1987 dioxin measurements are subject to bias from a possible violation of the half-life and first-order elimination assumptions that affect the initial dioxin estimates.

1.6.2 The Air Force Exposure Index

In the first three AFHS reports, summarizing results of physical examinations conducted in 1982, 1985, and 1987, the potential relation between health-related endpoints and herbicide exposure in Ranch Hand veterans was assessed using a calculated estimate of herbicide and dioxin exposure. This was called the Air Force exposure index.

The Air Force exposure index was calculated from military records to measure the potential exposure of a Ranch Hand to any of four dioxin-containing herbicides: Herbicides Orange, Purple, Pink, and Green. The index was only an estimate of dioxin exposure because the actual concentration of dioxin in the herbicides varied with type and lot and because exposure varied with individual work habits and duties. The calculation of the index was necessary because direct measures of dioxin exposure were not available at that time. Subsequent to 1987, all outcomes in this study have been assessed versus group contrasts and the dioxin body burden measured in serum. The 1987 results were analyzed twice, first using the Air Force exposure index (10), and then using the dioxin body burden as the measure of exposure (9).

The Air Force exposure index for a Ranch Hand was defined as the product of a dioxin weighting factor and the gallons of dioxin-containing herbicides sprayed during his tour divided by the number of men sharing his duties during his tour. This formula was based on the untested assumption that the exposure of an individual decreased as the number of men available increased. The calculation was performed for each month of his tour, and the monthly results were summed to produce a single exposure index for each Ranch Hand veteran. Each veteran was then assigned to a low, medium, or high exposure category depending on his calculated index and the tertiles of the index for his job category (officer-pilot, officer-navigator, officer-nonflying, enlisted flyer, or enlisted groundcrew). Additional details of the calculation are given in Thomas, et al. (10).

Both measures, the Air Force exposure index and the serum dioxin measurement, have limitations. The exposure index was approximate in that the number of gallons sprayed was based on the totals across all bases rather than at a specific base. In addition, the assumption that exposure decreased as the number of men available increased may not have been reasonable. Interviews with Ranch Hand groundcrew in 1989 revealed that as the workload increased, more men were added to the job, resulting in more men becoming exposed rather than each man becoming less exposed. Finally, the spectrum of behaviors, skills, duties, weather-related work stoppages, work surges due to war conditions, and other factors (some known, some unknown) were not included in the calculation. For example, some Ranch Hand groundcrew had direct contact with bulk quantities of herbicide by filling the tanks and servicing the equipment, while others drove trucks or forklifts away from the flight line. The index did not distinguish between these two kinds of exposure patterns. In addition, some Ranch Hands were assigned to administrative duties, which were indicated in their military records. The Air Force exposure index was defined as zero for those assigned to administrative duties.

The serum dioxin measurement is also limited as a measure of exposure. Although the half-life of dioxin is long (8.7 years), pharmacokinetic studies of Ranch Hand veterans suggest that the half-life varies with body fat (14). Thus, some veterans may eliminate dioxin quickly and others more slowly. Variation of

the dioxin half-life with body fat contributes to variation in the extrapolated initial dose at the time of exposure. In addition, more than 40 percent of Ranch Hand veterans have background levels, precluding extrapolation. Some of those with background levels may have had elevated levels while in Vietnam, while others may not have been occupationally exposed at all. The exposure status of Ranch Hands with background levels cannot be resolved with available data. Furthermore, no validated model exists with which to assess the adequacy of the estimated initial dose as an estimate of actual exposure among those with dioxin levels above background in 1987, 1992, or 1997. Use of serum dioxin measurements as a measure of exposure in Vietnam is further confounded by the other possible sources of dioxin exposure after service in Vietnam. These sources include industrial exposure and environmental factors such as fish consumption and burning of plastics.

The correlation between the Air Force exposure index and serum dioxin levels was described in the dioxin analysis of the 1987 physical examination results (9). These correlations reflected the high percentage of veterans who would be misclassified with regard to dioxin level if the Air Force exposure index was assumed as the standard. For example, 77 of 287 (26.8%) Ranch Hand veterans in the high Air Force exposure index category had dioxin levels less than 9 ppt (see Table 3.5 of reference 9).

Despite these limitations, the serum dioxin level appears to be the most appropriate measure of exposure in this study because of the following:

- It is a direct measurement of the contaminant.
- It has been accurately measured (16).
- It correlates with reported skin exposure to herbicides among enlisted Ranch Hand veterans (17).
- Its elimination in Ranch Hand veterans has followed a plausible pharmacokinetic pattern (14).
- It has been found plausibly associated with health conditions in this study and in other studies (12).

Throughout this report, dioxin levels are used as measures of both exposure to dioxin itself and exposure to dioxin-contaminated herbicides, including Herbicide Orange. Direct contrasts of Ranch Hand and Comparison veterans (Model 1) address the hypothesis of health effects attributable to any herbicide exposure experienced by Ranch Hand veterans during Operation Ranch Hand. Models involving dioxin measurements address the hypothesis that health effects change with the amount of exposure. Dioxin measurements are used as a measure of exposure to dioxin-contaminated herbicides because it is expected that as exposure to such herbicides increased, dioxin levels should increase. Therefore, the dioxin measurement serves as a direct biomarker of exposure to dioxin-contaminated herbicides. No other direct measure or estimate of herbicide exposure is available with which to address hypothetical dose-response relations with health. Some indirect measures, such as self-report of skin contact among enlisted groundcrew, or simply being a Ranch Hand enlisted groundcrew member, are valuable alternatives because dioxin measures suggest that enlisted groundcrew experienced the heaviest exposures. Reported skin exposure is not addressed in this report, but enlisted groundcrew status is addressed in Model 1. The use of dioxin as a measure of exposure to dioxin-contaminated herbicides is consistent with the goal of the study, which is to determine whether health effects exist and can be attributed to occupational exposure to Herbicide Orange (3).

1.6.3 Information Bias

Information bias, represented by the over- or under-reporting of disease symptoms, was minimized by verifying all diseases and conditions with medical records. It is possible that conditions in Ranch Hands may be more verifiable because they may have been seen by physicians more often than Comparisons.

This would be revealed by group differences in the quantity and content of medical records. Because there is no way to quantify these aspects, this potential source of bias remains unexplored. This bias, if it exists, would affect only the models contrasting Ranch Hands and Comparisons (Models 1 and 3) because Comparison data were not used in Models 2 and 4. Information bias due to errors in the data introduced through data entry or machine error is negligible. All laboratory results were subject to strict QC procedures, historical data were verified completely by medical records review, and medical data were subjected to strict QC standards (Chapter 6, Quality Control).

1.6.4 Consistency of Results

All statistically significant findings in this report were subjected to clinical review, ensuring internal consistency throughout the report. In addition, these findings were compared to published results from other studies to ensure external consistency.

1.6.5 Strength of Association

A strong adverse association between exposure and a disease condition, if it exists, would be revealed by an increased relative risk. Some authors have suggested that a statistically significant relative risk greater than 2.0 is cause for concern (18). Statistically significant relative risks less than 2.0 are generally considered to be less important than larger risks because relative risks less than 2.0 can arise more easily because of unrecognized bias or confounding. Relative risks greater than 5.0 are less subject to this concern. The numbers 2.0 and 5.0 are epidemiological guidelines regarding analyses of association between a dichotomous endpoint (disease, no disease) and exposure (yes, no). No such general guidelines have been formulated regarding the analysis of continuously distributed endpoints (such as cholesterol) versus continuously distributed exposure (such as initial or recent serum dioxin measurements).

Statistical power is also an issue in a study of a population this size. A study with a population of 2,121 lacks power to determine increases in relative risks for rare events (such as soft tissue sarcoma) because such events are unlikely to occur in large numbers in a group this small. While certain occupational toxins have a clear diagnostic pathology (e.g., mesothelioma for asbestos, hepatic angiosarcoma for vinyl chloride) virtually nonexistent in the absence of the toxin, other toxins merely increase the risk of nondiagnostic pathology. For example, this study would likely not discern an increase in the relative risk for a rare tumor that does not have a clear diagnostic pathology. By assessing the pathology observed in association with other known environmental risk factors (e.g., tobacco use, alcohol use), it is sometimes possible to provide a limit in the magnitude of effect missed; however, this study has inherent bounds in detecting modest increases in relative risk for infrequent pathology.

1.6.6 Biological Plausibility

The assessment of biological plausibility requires consideration of a biological mechanism relating the exposure and effect of interest. While a lack of biological credibility or even a contradiction of biological knowledge can lead to the dismissal of a significant result, the failure to perceive a mechanism may reflect only ignorance of the state of nature. On the other hand, it is easy to hypothesize biological mechanisms that relate almost any exposure to almost any disease. Thus, while important, the biological explanation of results must be interpreted with caution. In the AFHS, statistically significant results are subjected to medical review and comparison with previously published results in order to identify consistent and biologically plausible results.

1.6.7 Interpretation of Nonsignificant Results

In this study, a lack of significant results relating dioxin to a particular disease only means that the study is unable to detect a relation between dioxin and health. This does not imply that a relation may not exist, but that if it does exist, it was not detected. A lack of significant results does not mean that dioxin is safe or that there is no relation between dioxin and health. The AFHS was not designed to establish safety; rather, this study was designed to determine whether a hazard existed for the exposed personnel. Determination of safety would require a study at least 10 times as large, as determined in a 1985 study presenting minimal sample size criteria for proof of safety and hazard in studies of environmental and occupational exposures (13).

1.6.8 Extrapolation to Armed Forces Ground Troops

Extrapolation of the serum dioxin results to the general population of ground troops who served in Vietnam was difficult because Ranch Hand and ground troop exposure situations were very different. Based on serum dioxin testing results obtained by CDC (8) and others (19), nearly all ground troops tested had current levels of dioxin similar to background levels. Even combat troops who served in herbicide-sprayed areas of Vietnam had current levels similar to those in men who never left the United States (with mean dioxin levels of 4.2 ppt and 4.1 ppt, respectively). The AFHS subgroup most like the ground troops in terms of lipid-adjusted dioxin levels were the Ranch Hands who currently have background levels of dioxin. Therefore, if the results of the AFHS are applied to the general population of other Vietnam veterans, the focus should be on the "Background" Ranch Hand versus Comparison contrast. Extrapolating the results of these analyses to other Vietnam veterans still should be made cautiously, however. There may be demographic distinctions between the "Background" group of Ranch Hands and other Vietnam veterans that may be related to health. Also, if Ranch Hands with background levels of lipid-adjusted serum dioxin showed a significant adverse health effect relative to Comparisons, but if there was no significant effect for Ranch Hands with high serum dioxin levels, the plausibility of such an effect would be questionable, because this would not indicate a dose-response effect. In general, the analyses in this report found that Ranch Hands with background levels of lipid-adjusted dioxin did not show a significant adverse health effect relative to Comparisons.

1.6.9 Considerations for Summarizing Results

A study of this scope with a multitude of endpoints demands, and at the same time defies, meaningful summary tabulation. Such summaries can be misleading because they ignore correlations between the endpoints, correlations between study-examination results, and the nonquantifiable medical importance of each endpoint. In fact, many endpoints are correlated (e.g., psychological scales and indices developed from combining multiple variables). In addition, such tabulations combine endpoints that are not medically or biologically comparable. For example, diminished sense of smell is of less medical importance than the presence of a malignant neoplasm. Nevertheless, the AFHS presents a summary of all statistical results in Appendix G of this report. These summaries, however, can be misleading and must be interpreted carefully—an elementary tally of significant, or nonsignificant, results is not appropriate.

REFERENCES

1. Young, A. L., J. A. Calcagni, C. E. Thalken, and J. W. Tremblay. 1978. The toxicology, environmental fate, and human risk of herbicide orange and its associated dioxin. Technical Report OEHL-TR-78-92, USAF Occupational and Environmental Health Laboratory, Brooks Air Force Base, Texas. 247 pp.
2. Buckingham Jr., W. A. 1982. Operation Ranch Hand: the Air Force and herbicides in Southeast Asia, 1961-1971. Office of Air Force History, United States Air Force, Washington, DC. pp. 9-69, 199-201.
3. Lathrop, G. D., W. H. Wolfe, R. A. Albanese, and P. M. Moynahan. 1982. Epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Study Protocol. NTIS: AD A 122 250. USAF School of Aerospace Medicine, Brooks Air Force Base, Texas.
4. Centers for Disease Control. 1988. Serum 2,3,7,8-tetrachlorodibenzo-p-dioxin levels in Air Force Health study participants—preliminary report. *Morbidity and Mortality Weekly Report* 37:309-24.
5. DeStefano, F., O. J. Devine, W. D. Flanders, J. M. Karon, L. L. Needham, D. G. Patterson, and R. M. Worth. 1988. Serum 2,3,7,8-tetrachlorodibenzo-p-dioxin levels in U.S. Army Vietnam-era veterans. *Journal of the American Medical Association* 260:1249-54.
6. Lathrop, G. D., W. H. Wolfe, R. A. Albanese, and P. M. Moynahan. 1984. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Baseline morbidity study results. NTIS: AD A 138 340. USAF School of Aerospace Medicine, Brooks Air Force Base, Texas.
7. Pirkle, J. L., W. H. Wolfe, D. G. Patterson, L. L. Needham, J. E. Michalek, J. C. Miner, M. R. Peterson, and D. L. Phillips. 1989. Estimates of the half life of 2,3,7,8-tetrachlorodibenzo-p-dioxin in Vietnam veterans of Operation Ranch Hand. *Journal of Toxicology and Environmental Health* 27:165-71.
8. The Centers for Disease Control. 1988. Serum 2,3,7,8-tetrachlorodibenzo-p-dioxin levels in U.S. Army Vietnam-era veterans. *Journal of the American Medical Association* 260:1249-54.
9. Roegner, R. H., W. D. Grubbs, M. B. Lustik, A. S. Brockman, S. C. Henderson, D. E. Williams, W. H. Wolfe, J. E. Michalek, and J. C. Miner. 1991. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides. Serum Dioxin Analysis of 1987 Examination Results. NTIS: AD A 237 516-24. USAF School of Aerospace Medicine, Brooks Air Force Base, Texas.
10. Thomas, W. F., W. D. Grubbs, T. G. Karrison, M. B. Lustik, R. H. Roegner, D. E. Williams, W. H. Wolfe, J. E. Michalek, J. C. Miner, and R. W. Ogershok. 1990. The Air Force Health Study. An Epidemiologic Investigation of Health Effects in Air Force Personnel Following Exposure to Herbicides. 1987 Followup Examination Results, May 1987 to January 1990. NTIS: AD A 222 573. USAF School of Aerospace Medicine, Brooks Air Force Base, Texas.
11. Burton, J. E., J. E. Michalek, and A. J. Rahe. 1998. Serum Dioxin, Chloracne, and Acne in Veterans of Operation Ranch Hand. *Archives of Environmental Health* 199-200.

12. Institute of Medicine. 1999. *Veterans and Agent Orange. Update 1998.* National Academy Press. Washington, DC.

13. Bross, I. D. 1985. Proof of safety is much more difficult than proof of hazard. *Biometrics* 41:785-93.

14. Michalek, J. E., J. L. Pirkle, S. P. Caudill, R. C. Tripathi, D. G. Patterson Jr., and L. L. Needham. 1996. Pharmacokinetics of TCDD in veterans of Operation Ranch Hand: 10-year follow-up. *Journal of Toxicology and Environmental Health* 47:209-20.

15. Needham, L. L., P. M. Gerthoux, D. G. Patterson Jr., P. Brambilla, W. E. Turner, C. Beretta, J. L. Pirkle, L. Colombo, E. J. Sampson, P. L. Tramacere, S. Signorini, L. Meazza, V. Carreri, R. J. Jackson, and P. Mocarelli. 1997-98. Serum dioxin levels in Seveso, Italy, population in 1976. *Teratogenesis, Carcinogenesis, and Mutagenesis* 17(4-5):225-40.

16. Michalek, J. E., R. C. Tripathi, P. M. Kulkarni, and J. L. Pirkle. 1996. The reliability of the serum dioxin measurement in veterans of Operation Ranch Hand. *Journal of Exposure Analysis and Environmental Epidemiology* 6(3):327-38.

17. Michalek, J. E., W. H. Wolfe, J. C. Miner, T. M. Papa, and J. L. Pirkle. 1995. Indices of TCDD exposure and TCDD body burden in veterans of Operation Ranch Hand. *Journal of Exposure Analysis and Environmental Epidemiology* 5:209-23.

18. Breslow, N. E., and N. E. Day. 1980. *Statistical methods in cancer research.* Lyon, France: International Agency for Research on Cancer.

19. Kahn, P. C., M. Gochfeld, M. Nygren, M. Hansson, C. Rappe, H. Velez, T. Ghent-Guenther, and W. P. Wilson. 1988. Dioxins and dibenzofurans in blood and adipose tissue of Agent Orange-exposed Vietnam veterans and matched controls. *Journal of the American Medical Association* 259:1661-7.

Table of Contents

List of Tables

List of Figures

2 THE DIOXIN ASSAY

2.1 PARTICIPANTS SELECTED FOR DIOXIN MEASUREMENT

The eligibility for participants at the 1997 physical examination to have a blood measurement of dioxin was determined by assignment to one of three categories: (a) previous participants with a quantitative dioxin result who were selected for an additional blood measurement of dioxin to advance pharmacokinetic studies (1), (b) previous participants returning to the 1997 physical examination with no prior dioxin blood measurement or no previously quantitative dioxin results, and (c) first-time participants. Of the 2,121 participants at the 1997 follow-up examination, a total of 594 participants were asked to provide a blood sample for use in analysis of serum dioxin levels. Table 2-1 shows the number of participants selected for the 1997 dioxin blood measurement belonging to each category by exposure group (Ranch Hand, Comparison). Table 2-1 also gives the number of actual dioxin assay results obtained that belonged to each category by exposure group.

Table 2-1. Participants with a 1997 Blood Measurement of Dioxin

Category	Number Eligible			Number of Results		
	Ranch Hand	Comparison	Total	Ranch Hand	Comparison	Total
Returning participants with a previous quantitative dioxin result selected for another blood measurement of dioxin to advance pharmacokinetic studies	430	0	430	421	0	421
Returning participants who either attended the 1987 or 1992 follow-ups but had no previous dioxin blood measurement or no previous quantitative dioxin result	18	42	60	17	40	57
Participants who were selected for a dioxin blood measurement for the first time	11	93	104	5	80	85
Total	459	135	594	443	120	563

Table 2-2 displays the reasons why blood samples from 31 participants were not obtained. Nine participants were medically deferred because of pending surgery or a low hemoglobin level, and 22 participants refused the blood measurement of dioxin. Samples for the remaining 563 participants were shipped to the Centers for Disease Control and Prevention (CDC) for analysis.

Table 2-2. Participants Eligible for the 1997 Blood Measurement of Dioxin and Reasons for Participant Sample Exclusions

Distribution of Sample Exclusion	Ranch Hand	Comparison	Total
Total Eligible for Blood Measurement of Dioxin	459	135	594
Less:			
Medically Deferred	(7)	(2)	(9)
Refused	(9)	(13)	(22)
Total Specimens Sent to CDC	443	120	563

2.2 SAMPLE ACQUISITION

Following a CDC protocol, blood was drawn from consenting participants for the serum dioxin assay on the morning of the second day of the 1997 physical examination. The participants were instructed to fast after midnight (water was allowed), and samples were drawn with a 15-gauge needle into a blood pack unit without anticoagulant. CDC purchased blood bags in lots of 1,200, packaged in 50 boxes of 24 bags per box, and tested one bag per box to assess dioxin contamination. If the tested bag was found to be free of dioxin contamination, the box of 24 bags was shipped to the Air Force for use in the study.

Participants had 280 ml of blood drawn. After the draw, the bags were clamped, labeled, placed upright, and the samples were allowed to clot at room temperature for 7 hours.

The clotted samples were centrifuged for 15 minutes at 4,500 revolutions per minute between 4° and 10 °C. The serum was then transferred from the spun unit bag by a plasma extractor to transfer packs that also were tested and found to be free of dioxin. The transfer packs were then spun for 15 minutes at 4,500 revolutions per minute. The serum was placed into four Wheaton bottles: two 4-ounce bottles for the serum dioxin analysis, a 5 ml bottle for the lipid profile, and a 10 ml bottle for the reserve serum. Samples were catalogued and stored at –70 °C or colder until shipment. Appendix A contains the detailed procedures used by Scripps Clinic for the dioxin blood collection and processing. Frozen samples were packed in dry ice in Styrofoam boxes and shipped weekly from Scripps Clinic in La Jolla, California, to Brooks Air Force Base, Texas. At Brooks Air Force Base, inventory was taken and the specimens were stored at –70 °C until shipment to CDC. All samples were coded so that the CDC staff was blinded to the exposure group status (Ranch Hand, Comparison) of each specimen.

2.3 ANALYTICAL METHOD

The serum samples were analyzed for dioxin in groupings consisting of a method blank, three unknown samples, and a quality control (QC) pool sample (2, 3). Cholesterol esters, triglycerides, and high-density lipoprotein cholesterol were determined in duplicate by standard methods. Total phospholipids were determined in duplicate by modifying the Folch, et al., procedure (4, 5). Free cholesterol was determined in duplicate by an enzymatic method (6). For each analysis, the mean result of duplicate analyses was used to calculate the concentrations of total lipids using the summation method (7), low-density lipoprotein cholesterol, and very low-density lipoprotein cholesterol (8).

2.4 QUALITY CONTROL

Quality assurance was maintained with matrix-based materials well characterized for dioxin concentration and isotope ratios to ensure that the analytical system was in control. QC charts were maintained for each of these materials (five serum pools). The concentration in the QC sample from each analytical run was

required to be within established 99-percent confidence limits (9, 10). The unlabeled and carbon-13 labeled internal standard isotope ratios were required to be within 95-percent confidence limits. All analytical runs for the dioxin and lipid measurements were in control. No dioxin was detected in the blanks (on-column injection of 100 femtograms from a standard solution produces detectable signals greater than three times the background noise).

2.5 DATA DESCRIPTION

CDC delivered whole-weight and lipid-adjusted dioxin concentrations to the Air Force, together with the total sample weight, weights of lipid fractions, total lipid weight, detection limit, quantitation limit, and all associated QC information, including results from blank samples. The lipid-adjusted dioxin concentration was calculated using the whole-weight dioxin concentration and the total lipid weight. Details of the calculation are discussed subsequently in this chapter. Table 2-3 provides the results of the 1997 physical examination blood measurements of dioxin by exposure group and result comment. Result comments are based on whether the result was measurable, or good, (G); measurable, but below the limit of detection (GND) or below the limit of quantitation (GNQ); or no result was obtained (NR).

Table 2-3. Result Comments for the 1997 Blood Measurements of Dioxin

Result Comment	Ranch Hand	Comparison	Total
Good Result (G)	430	82	512
Good Result, Below Limit of Detection (GND)	11	35	46
Good Result, Below Limit of Quantitation (GNQ)	0	0	0
No Result (NR)	2	3	5
Total	443	120	563

Note: The two Ranch Hands with no result at the 1997 follow-up examination had a good result at a previous follow-up examination.

The Air Force Health Study (AFHS) dioxin database is a combination of the dioxin assay results from the 1987, 1992, and 1997 examinations. Table 2-4 shows the number of blood measurements of dioxin by year and illustrates the high percentage of study participants who have had dioxin measurements. Of the 2,121 fully compliant participants for the 1997 study, 2,101 (99.1%) had blood measurements of dioxin in 1997 or in a previous study.

Table 2-4. Dioxin Results for 1997 Physical Examination Participants

Years of Dioxin Blood Measurement Result	Ranch Hand	Comparison	Total
No Dioxin Blood Measurement	6	14	20
1987 Only	297	865	1,162
1992 Only	56	118	174
1997 Only	12	93	105
1987 and 1992	68	134	202
1987 and 1997	153	6	159
1992 and 1997	5	7	12
1987, 1992, and 1997	273	14	287
Total	870	1,251	2,121

Note: 1987 includes participants from both the 1987 pilot study and the 1987 follow-up physical examination.

Participants may have been assayed during any combination of four events: the pilot study conducted in April 1987 (9), the 1987 follow-up examination (May 1987 to March 1988), the 1992 follow-up examination (May 1992 to March 1993), or the 1997 follow-up examination (May 1997 to April 1998). The majority of participants had an assay in 1987, through either the pilot study or the 1987 follow-up examination. Consequently, 1987 was designated as the reference point for post-Southeast Asia (SEA) serum dioxin levels, termed "current dioxin" in previous AFHS reports and "1987 dioxin" subsequently in this report.

Each participant with a good (G or GND) dioxin result was given a "reference" dioxin assay result derived from the good result. When a participant had multiple assay results, first priority was given to the 1987 pilot-study dioxin results, second priority was given to results derived from serum collected at the 1987 physical examination, third priority was given to the 1992 results, and fourth priority was given to the 1997 results. Figure 2-1 outlines this decision process and shows that the first quantitative result was used.

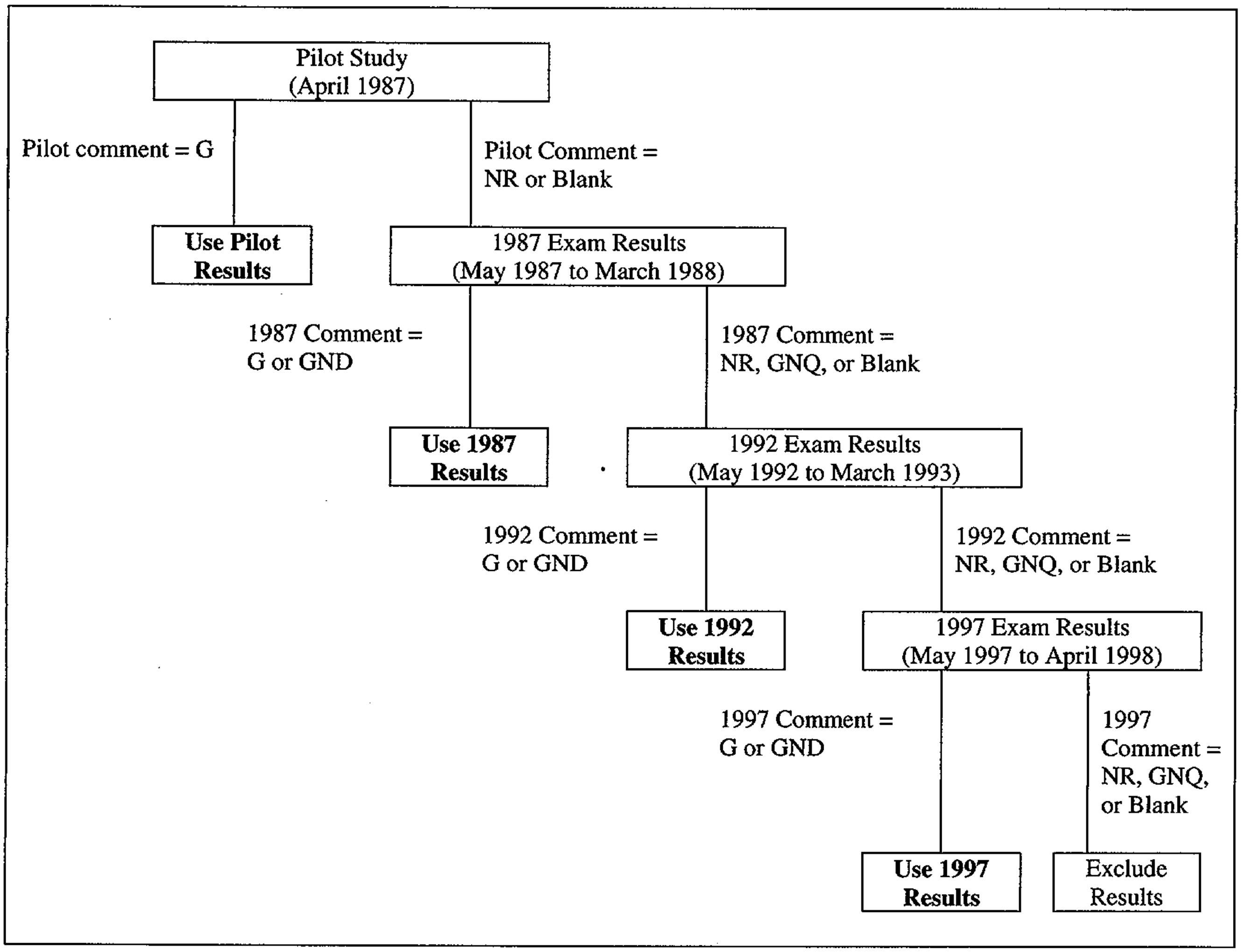

Figure 2-1. Decision Process for Determination of Dioxin Results for Analysis

Of the 2,121 fully compliant participants at the 1997 physical examination, 870 were Ranch Hands and 1,251 were Comparisons. Of the 2,121 participants, 20 had never had blood measured for dioxin. Six participants had missing dioxin results (result comment = NR) or nonquantitative dioxin results (result comment = GNQ). A total of 2,095 participants, consisting of 863 Ranch Hands and 1,232 Comparisons, had quantitative dioxin measurements. Table 2-5 summarizes the sample sizes by exposure group. The six participants with missing or nonquantitative dioxin results are cross-classified in Table 2-6 by result comment and exposure group.

Table 2-5. Results from Blood Measurements of Dioxin

Summary of Sample Size Reduction	Ranch Hand	Comparison	Total
1997 Follow-up Participants	870	1,251	2,121
Less: No Blood Measurement of Dioxin at any Physical Examination	(6)	(14)	(20)
1997 Follow-up Participants with a Dioxin Assay	864	1,237	2,101
Less: Missing or Nonquantitative (Good Result, but Below Limit of Quantitation or No Result)	(1)	(5)	(6)
1997 Follow-up Participants with Quantitative Dioxin Results	863	1,232	2,095

Table 2-6. Results from Blood Measurements of Dioxin with Missing or Nonquantitative Results

1987 Assay	1992 Assay	1997 Assay	Ranch Hand	Comparison	Total
GNQ			1	1	2
GNQ	GNQ		0	1	1
GNQ		NR	0	1	1
		NR	0	2	2
Total			1	5	6

Note: GNQ = Good result, below level of quantitation.
NR = No Result.

If the 1987 pilot study or follow-up measurement was not used, the 1987 dioxin level was derived for each participant in the following manner. If the 1992 measurement was used, the level was extrapolated to 1987 levels when the 1992 dioxin concentration surpassed 10 parts per trillion (ppt). These extrapolated lipid-adjusted dioxin values were calculated using a first-order elimination model with a half-life of 8.7 years and a background level of 4 ppt. Levels at or below 10 ppt were not extrapolated because the first-order elimination model was not considered to be valid at background levels (lipid-adjusted 1987 dioxin levels ≤10 ppt). If the 1997 measurement was used, the level was extrapolated to 1987 levels when the 1997 dioxin concentration surpassed 10 ppt. Details on the extrapolation method are given in Chapter 7, Statistical Methods. A summary detailing the year the measurement was used and whether the dioxin level was extrapolated to 1987 dioxin levels is provided in Table 2-7 by exposure group.

Table 2-7. Summary of Number of Assays Used for 1997 Follow-up Participant Dioxin Measures

Study	Ranch Hand		Comparison		Total	
Pilot (1987)	127		44		171	
1987 Follow-up	615		858		1,473	
1992 Follow-up	99		213		312	
Extrapolated to 1987		35		0		35
Not Extrapolated to 1987		64		213		277
1997 Follow-up	22		117		139	
Extrapolated to 1987		4		0		4
Not Extrapolated to 1987		18		117		135
Total	863		1,232		2,095	

2.6 LIPID-ADJUSTED AND WHOLE-WEIGHT CURRENT DIOXIN MEASUREMENTS

Serum dioxin is defined as the serum concentration of 2,3,7,8-tetrachlorodibenzo-p-dioxin (dioxin). It can be expressed as a lipid-adjusted or a whole-weight measurement. The lipid-adjusted dioxin measurement, also called "current dioxin body burden," is a derived quantity calculated from the formula $ppt = ppq \cdot 102.6/W$, where ppt is the lipid-adjusted concentration, ppq (parts per quadrillion) is the actual weight of dioxin in the sample (also known as whole-weight dioxin) in femtograms, 102.6 corrects for the average density of serum, and W is the total lipid weight of the sample (10).

The correlation between the serum lipid-adjusted concentration and adipose tissue lipid-adjusted concentration of dioxin has been observed to be 0.98 in 50 persons from Missouri (11). Using the same data, Patterson, et al., calculated the partitioning ratio of dioxin between adipose tissue and serum on a lipid-adjusted basis as 1.09 (95% confidence interval: [0.97,1.21]). On the basis of these data, a one-to-one partitioning ratio of dioxin between lipids in adipose tissue and lipids in serum cannot be excluded. Measurements of dioxin in adipose tissue generally have been accepted as representing the body burden concentration of dioxin. The high correlation between serum dioxin levels and adipose tissue dioxin levels in the study by Patterson, et al., suggests that serum dioxin is also a valid measurement of dioxin body burden.

Figures 2-2 and 2-3 show the distribution of serum lipid-adjusted dioxin for the 863 Ranch Hands and 1,232 Comparisons whose results were used in analyses of 1987 dioxin versus health in this report. Figure 2-4 compares distributions of serum lipid-adjusted dioxin concentrations for Ranch Hands and Comparisons on the same scale (parts per trillion). Figure 2-5 compares distributions of the logarithm (base 2) of serum lipid-adjusted dioxin concentrations for Ranch Hands and Comparisons on the same scale.

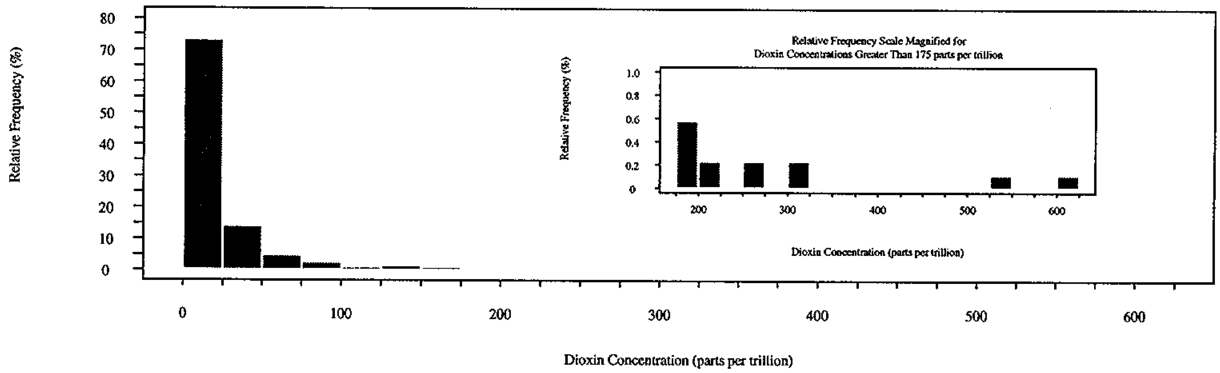

Figure 2-2. Relative Frequency Distribution of Lipid-adjusted Dioxin Concentrations for 863 Ranch Hands

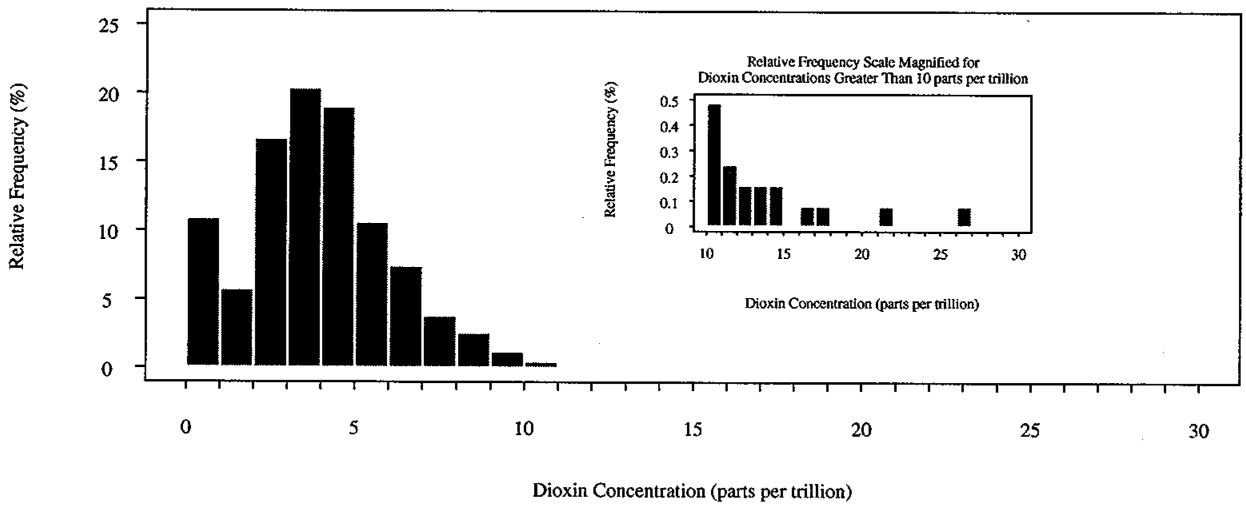

Figure 2-3. Relative Frequency Distribution of Lipid-adjusted Dioxin Concentrations for 1,232 Comparisons

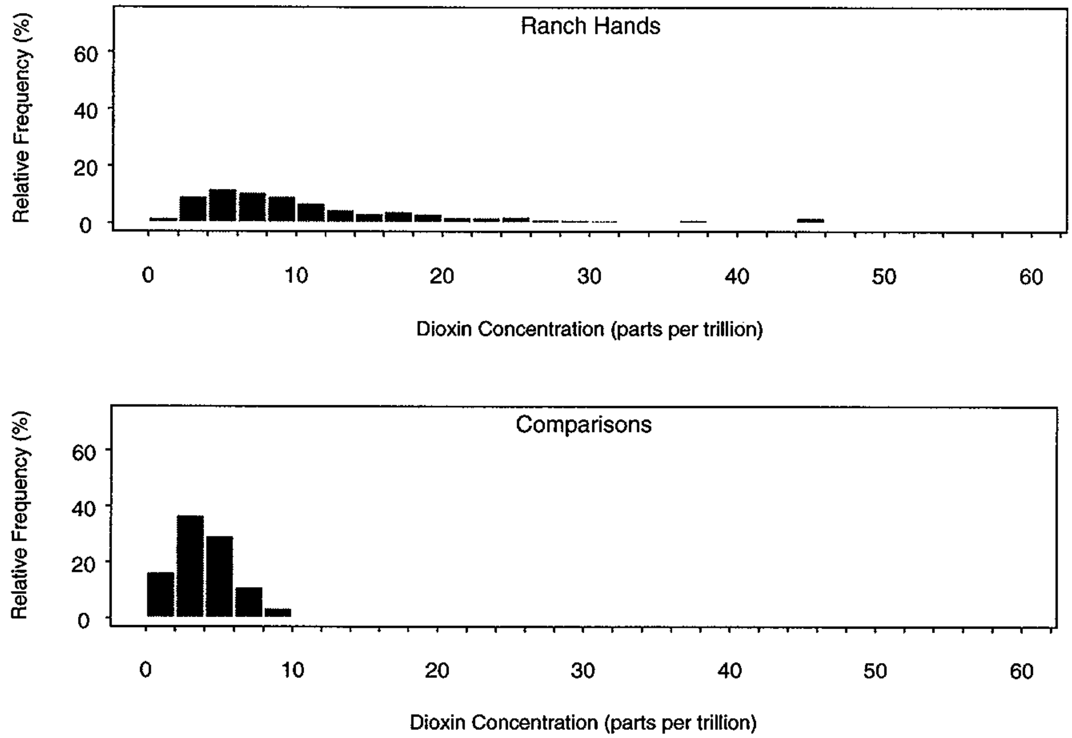

Figure 2-4. Relative Frequency Distribution of Lipid-adjusted Dioxin Concentrations

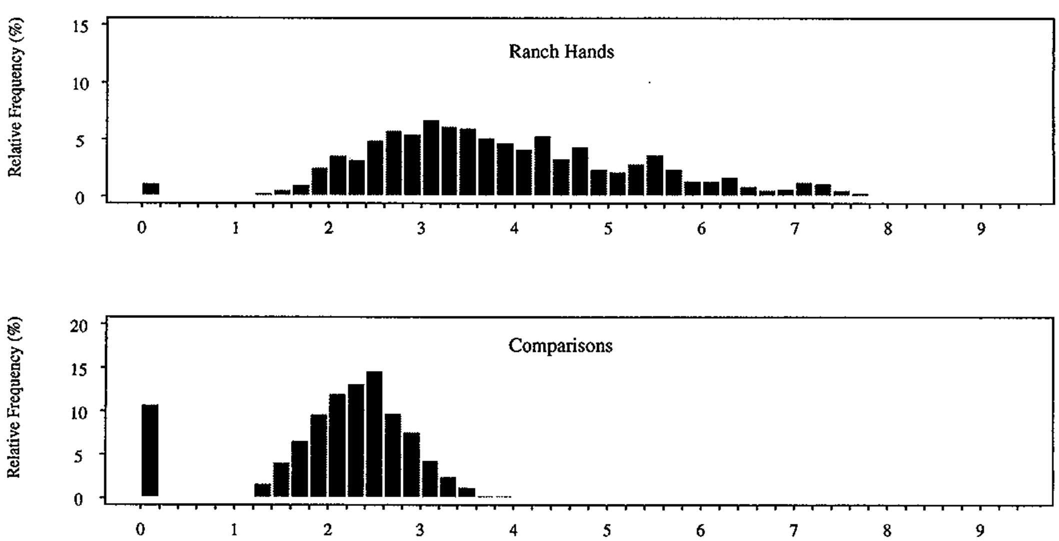

Figure 2-5. Relative Frequency Distribution of the Logarithm (Base 2) of Lipid-adjusted Dioxin Concentrations

Table 2-8 summarizes, by military occupation and exposure group, the serum lipid-adjusted dioxin results among the 863 Ranch Hands and 1,232 Comparisons whose results were used in the analyses of dioxin versus health in this report. For Ranch Hands, the median level was greatest for enlisted groundcrew and least for officers.

Table 2-8. Lipid-adjusted Dioxin Result Summary

	Ranch Hand			Comparison		
Military Occupation	n	Median (ppt)	Range (ppt)	n	Median (ppt)	Range (ppt)
Officer	337	7.4	0-36.0	486	4.0	0-17.3
Enlisted Flyer	151	16.4	0-195.5	186	3.8	0-12.8
Enlisted Groundcrew	375	24.0	0-617.8	560	3.6	0-26.6
Total	863	11.6	0-617.8	1,232	3.8	0-26.6

Note: ppt = parts per trillion.

2.7 SUMMARY

In summary, serum was collected for dioxin analysis for 563 participants at the 1997 follow-up at Scripps Clinic. The serum was shipped from Scripps Clinic to Brooks Air Force Base to CDC according to rigid protocols. The data collected from the 1997 follow-up assays were combined with data from the 1987 pilot study, 1987 follow-up examination, and 1992 follow-up examination for use in pharmacokinetic studies and for determining post-SEA dioxin levels. After combining data from this and previous follow-ups, a total of 863 of the 870 Ranch Hands (98.5%) and 1,232 of the 1,251 Comparisons (99.1%) attending the 1997 follow-up examination had quantitative dioxin assay results.

REFERENCES

1. Michalek, J. E., J. L. Pirkle, S. P. Caudill, R. C. Tripathi, D. G. Patterson Jr., and L. L. Needham. 1996. Pharmacokinetics of TCDD in Veterans of Operation Ranch Hand: 10-year Follow-up. *Journal of Toxicology and Environmental Health* 47:209-20.
2. Patterson Jr., D. G., J. S. Holler, C. R. Lapeza Jr., L. R. Alexander, D. F. Groce, R. C. O'Conner, S. J. Smith, J. A. Liddle, and L. L. Needham. 1986. High resolution gas chromatographic/high resolution mass spectrometric analysis of human adipose tissue for 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Annals of Chemistry* 58:705-13.
3. Patterson Jr., D. G., L. Hampton, C. R. Lapeza Jr., W. T. Belser, V. Green, L. R. Alexander, and L. L. Needham. 1987. High resolution gas chromatographic/high resolution mass spectrometric analysis of human serum on a whole weight and lipid weight basis for 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Annals of Chemistry* 59:2000-05.
4. Beveridge, J., and S. Johnson. 1949. The determination of phosolipid phosphorous. *Canadian Journal* 27E:159-63.
5. Folch, J., M. Lees, and G. H. Sloan-Stanley. 1957. A simple method for the isolation and purification of total lipids from animal tissue. *Journal of Biology and Chemistry* 226:497-509.
6. Cooper, G. R., P. H. Duncan, J. S. Hazelhurst, D. T. Miller, and D. D. Bayse. 1982. Cholesterol, enzymic method. In Vol. 9, *Selected methods for the small clinical chemistry laboratory*, ed. W. E. Faulkner and S. Meites. Washington, DC: American Association for Clinical Chemistry.
7. Cheek, C. S., and D. F. Wease. 1969. A summation technique for serum total lipids: comparison of methods. *Clinical Chemistry* 15:102-7.
8. Friedewald, W. T., R. I. Levy, and D. S. Fredrickson. 1972. Estimation of the concentration of low density lipoprotein cholesterol in plasma, with use of the preparative centrifuge. *Clinical Chemistry* 18:499-502.
9. Wolfe, W. H., J. E. Michalek, J. C. Miner, and M. R. Petersen. 1988. Serum 2,3,7,8-tetrachlorodibenzo-p-dioxin levels in Air Force Health Study participants. Preliminary report. *Morbidity and Mortality Weekly Report* 37:309-11.
10. Akins, J. R., K. Waldrep, and J. T. Bernert Jr. 1989. The estimation of total serum lipids by a completely enzymatic "summation" method. *Clinica Chimica Acta* 184:219-26.
11. Patterson, D. G., L. L. Needham, J. L. Pirkle, D. W. Roberts, J. Bagby, W. A. Garrett, J. S. Andrews Jr., H. Falk, J. T. Bernert, E. J. Sampson, and V. N. Houk. 1988. Correlation between serum and adipose tissue levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin in 50 persons from Missouri. *Archives of Environmental Toxicology* 17:139-43.

Table of Contents

3 QUESTIONNAIRE METHODOLOGY

This chapter describes the development and implementation of the two participant questionnaires used in the 1997 follow-up to the Air Force Health Study (AFHS): the 1997-98 Health Interval Questionnaire and the 1997-98 Study Subject Baseline Questionnaire. Both questionnaires were formatted and administered by the National Opinion Research Center (NORC), a social science research center at the University of Chicago.

The two 1997 questionnaires were comparable to those used in the baseline study and the 1985, 1987, and 1992 follow-up efforts. In the 1982 baseline study, interviews were conducted in the participants' homes. In the 1985, 1987, and 1992 studies, the follow-up interviews were conducted in person at the physical examination site. The latter method proved to be more efficient and subject to better quality control (QC). In all the examinations before 1997, the questionnaires were administered in hard copy, which was later edited and key-entered into the final SAS®[1] data set. For the 1997 follow-up, the interview responses were recorded electronically on laptop computers using a computer-assisted personal interviewing (CAPI) system. This method afforded an added measure of QC.

The baseline questionnaire was administered to any participant who had not previously completed that questionnaire. With the exception of the translation into the CAPI format, the baseline questionnaire has not changed since 1982. The interval questionnaire was designed to capture the participant's health history in the interval since participation in previous follow-up examinations. In addition, the interval questionnaire elicited general health measures needed by the debriefing physicians.

3.1 QUESTIONNAIRE DEVELOPMENT

An objective of questionnaire development in each follow-up year has been to maintain, to the maximum extent possible, the question wording, context, and procedures used in the 1982 baseline study. In addition, the interval questionnaire was often augmented to obtain data on new areas of inquiry. The central task of questionnaire development has been to obtain interval histories on questionnaire items, thereby updating the information provided in previous follow-up studies. For instance, if a study subject participated in the 1992 follow-up, the 1997-98 Health Interval Questionnaire elicited an interval history for the period from 1992 to 1997; however, if the subject last participated in the baseline study or the 1985 follow-up, the 1997-98 Health Interval Questionnaire elicited an interval history from those dates until 1997.

3.1.1 Baseline Questionnaire

The baseline questionnaire used during the 1997 examination was developed in 1982 and has never been changed. The 1982 Study Subject Baseline Questionnaire obtained information on demographics, education, occupation, medical history, study compliance, toxic exposures, and reproductive history. In general, responses to histories and other questions where the response does not change over time were obtained in the baseline questionnaire. Each participant completed the baseline questionnaire the first time he participated in the study. In the 1997 follow-up study, no changes were made to the content of the baseline questionnaire.

[1] SAS and all other SAS Institute, Inc., product and service names are registered trademarks or trademarks of SAS Institute, Inc., in the USA and other countries.

3.1.2 Interval Questionnaire

All participants were asked questions to update their history from previous interviews. These data were obtained in the interval questionnaire. For the 1985 follow-up, new questions on risk factors for skin cancer and personality type were added. Enhancements were added to the data collection procedures to include birth defects and drinking habits, and questions were included to obtain a more detailed smoking history. The interval questionnaire was expanded in 1987 to include detailed drinking history and sleep disorder questions. Because some of the study subjects did not participate in the 1985 follow-up, the 1987-88 Health Interval Questionnaire was structured to include one-time questions added in 1985, such as ethnic background and smoking history, for "rejoining" participants (i.e., those who completed a previous questionnaire but did not participate in all examinations).

The 1992-93 Health Interval Questionnaire added questions concerning occupational exposure to heavy metals and vibrating power tools, family health history (with particular reference to diabetes, heart trouble, and heart disease), further participant health inquiries (in particular, questions about diabetes, hepatitis B, intermittent claudication, and vascular insufficiency), and the participant's normal level of physical activity. In addition, the 1992 participants completed a Diet Assessment Questionnaire developed by Walter Willett at Harvard University (1).

With the exception of the diet assessment, which was discontinued for the 1997 follow-up, the 1997-98 Health Interval Questionnaire contained all of the questions in the 1992-93 Health Interval Questionnaire, the Interval Supplement Recording Book, and AFHS Forms 1, 1B, 2A, and 8 (the "self-administered" forms). The 1997-98 Health Interval Questionnaire also added the two following questions on herbicide exposure:

- What percentage of the missions that you flew as part of the aircrew during the Ranch Hand operation were herbicide spraying missions?

- It has been reported that some Vietnam veterans have intentionally drunk herbicides. Have you ever intentionally drunk herbicides?

Copies of the 1992-93 Health Interval Questionnaire and the Interval Supplement Recording Book are provided in Appendix B of the 1992 Final Report (2). AFHS Forms 1, 1B, 2A, and 8 are provided in Appendix C of the same report.

The goals in developing the CAPI Interval Questionnaire for the 1997 follow-up survey included the following:

1. To create one questionnaire encompassing the interval questionnaires and the "self-administered" forms. Questions from the additional forms were inserted throughout the questionnaire into sections covering similar subjects.
2. To print health history responses, previously available from the self-administered forms, onsite after the interview for use in participant debriefing.
3. To eliminate item nonresponse.
4. To use "bounded recall" techniques to improve participants' abilities to recall information. A longitudinal questionnaire is dependent on the respondent's ability to remember events and to place those events in time. Even when given a precise starting date, respondents frequently repeat information given earlier, neglect to report new information because they thought they had previously reported it, and otherwise misplace events in time or forget them completely. One

method of preventing such errors is through the use of "bounded recall," in which the respondent is reminded of information that he has already reported and asked to provide new information. For the 1992 interview, interviewers worked from a hard-copy information sheet containing summaries of key responses from the previous examination. These responses included date of birth, highest educational degree, military status at the last interview, marital status at the last interview, name of spouse or partner at the last interview, and a cumulative list of all children reported during previous interviews. This practice was replicated online for the 1997 questionnaire.

5. To minimize redundancies of items asked of participants and to avoid reminders of previously reported sensitive family history items during their interview. These goals were accomplished by including the items from the self-administered forms in the CAPI questionnaire and by programming the CAPI questionnaire to skip any sensitive family history items, such as parents or children previously reported as deceased.
6. To replicate, to the maximum extent possible, the 1992 variables, names, labels, and formats in the final SAS® data set.
7. To lessen the time burden on the participant for the administration of the questionnaires. By combining the self-administered forms with the interval questionnaire and reducing the redundancy of questions, the participants were able to complete this portion of their examinations in a timelier manner.

3.2 INTERVIEWER TRAINING

In April 1997, NORC's Chicago office staff trained eight interviewers and one field manager to administer the 1997-98 Health Interval and Study Subject Baseline Questionnaires. One interviewer and the Field Manager had administered questionnaires previously in the 1992 follow-up examination. The interviewers reported to the Field Manager, who in turn reported to the Data Collection Task Leader in Chicago. The Field Manager observed interviews by each interviewer and presented summaries of these assessments each quarter. The NORC Project Director made quarterly visits to the interviewing site. As part of the training process, the NORC interviewing staff was not informed of the exposure status of any study participant either before or after questionnaire completion.

3.3 DATA COLLECTION

Upon arrival at Scripps Clinic, the participant received a schedule that included the time and place for the interval interview (and, if appropriate, the baseline interview) and was assigned an interviewer. In all of the personal interviews conducted for the AFHS, interviewers were required to ask questions exactly as written, were not allowed to interpret questions or interject personal commentary, and were instructed to probe "Don't Know" responses at least once. As an added QC measure, the CAPI system did not permit them to skip around among sections of the questionnaire.

During the interview, participants signed both informed consent and medical records release forms. If a participant did not have all of the information with him to complete the medical release form during the interview, he was given blank medical records release forms and instructed to mail the completed forms to the Air Force. If the medical records required pertained to his now-adult children and required their signature, he was again given blank medical records release forms and instructed to mail the completed forms to the Air Force. During the course of the data collection, the interviewing procedures were amended so that medical release forms were not signed if the participant informed the interviewer that he

had brought the relevant records with him, that the records had already been submitted to the AFHS, or that the condition had been diagnosed at Scripps Clinic.

After each interview, interviewers used an onsite printing program that was built into the CAPI system to produce a six-page form containing items from the questionnaire that were needed for the participant debriefings. These forms were transferred to the participants' folders each day. Each evening, the completed interviews were uploaded via modem to the NORC home office in Chicago. At that time, new participant data and refinements to the questionnaire software also could be downloaded to the interviewing site.

REFERENCES

1. Willett, W. C., R. D. Reynolds, S. Cottrell-Hoehner, L. Sampson, and M. L. Brown. 1987. Validation of a Semi-quantitative Food Frequency Questionnaire: Comparison with a One-year Diet Record. *Journal of the American Dietetic Association* 87(1):43-7.

2. Grubbs, W. D., W. H. Wolfe, J. E. Michalek, D. E. Williams, M. B. Lustik, A. S. Brockman, S. C. Henderson, F. R. Burnett, R. G. Land, D. J. Osborne, V. K. Rocconi, M. E. Schreiber, J. C. Miner, G. L. Henriksen, and J. A. Swaby. 1995. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final Report. 1992 Followup Examination Results. NTIS: AD A 304 306, 304 308-316. United States Air Force School of Aerospace Medicine, Brooks Air Force Base, Texas.

Table of Contents

List of Tables

List of Figures

4 PHYSICAL EXAMINATION METHODOLOGY

The 1997 follow-up examination was given to 2,121 invited and scheduled participants, who traveled to the examination site at Scripps Clinic in La Jolla, California. The examination consisted of the following major elements:

- Adipose tissue extraction
- Laboratory testing
- Medical outbriefings
- Physical examination
- Psychological testing
- Specialized testing (e.g., phlebotomy for measurement of serum dioxin).

The Combat Experience Questionnaire and skin, hair, and eye color determinations (components of the 1985 follow-up examination) were administered to all participants who did not attend the 1985, 1987, and 1992 follow-up examinations.

The Air Force carefully prescribed the details of the above examination elements in the Examiners' Handbook, provided in Appendix B. All physical examination procedures were approved by the Air Force Research Laboratory Institutional Review Board (IRB) at Brooks Air Force Base and by the Scripps Clinic IRB. Clinical variations were neither desired nor authorized; all proposed examination procedural changes were reviewed in detail by Air Force technical and contractual personnel prior to the start of the examinations. An important objective of the entire physical examination process was to ensure that bias was not created by any procedural change. This objective was carried out successfully.

The requirement to maintain blind examinations was particularly stringent. The clinical staff was prohibited from knowing or seeking information as to the group identity (i.e., Ranch Hand, Comparison) of any participant. At the end of his examination, each participant was asked to note on the critique form whether such information was sought by any member of the clinical or paramedical staff. In 1997, nine participants indicated that an examining physician had asked them about specific duties in Southeast Asia (SEA). Two of these participants later stated that they had answered erroneously. Three participants stated that they had not been questioned but rather had volunteered information in casual conversation. The balance of the nine participants could not be identified because they chose to remain anonymous. In all known cases, the physician or technician involved was reminded to be more careful in his or her conversations.

4.1 EXAMINATION CONTENT

The examination content, as designed by the Air Force, emphasized detection of medical endpoints suspected of being associated with exposure to phenoxy herbicides, chlorophenols, or dioxin. In each follow-up study, the Air Force has used findings from the previous examination to refine the current examination.

The general content of the 1997 physical examination and psychological test battery is shown in Table 4-1. The complete laboratory test series accomplished at Scripps Clinic is displayed in Table 4-2.

Table 4-1. Elements of the 1997 Follow-up Physical Examination

Elements	Remarks
Adipose Tissue Extraction	313 Participants
Chest X Ray	Radiologist
Dermatologic Examination	Dermatologist
Doppler	Technician; Caffeine and Nicotine Abstinence
Electrocardiogram	Caffeine and Nicotine Abstinence
General Physical Examination	Internist
Immunologic Studies	40% Random Sample
Neurological Examination	Neurologist
Patient Outbriefing	Internist, Medical Diagnostician
Psychological Evaluation:	
Symptom Checklist 90-Revised (SCL-90-R)	
Jenkins Activity Survey	
Pulmonary Function	Internist with Subspecialty in Pulmonary Disease
Vibrotactile Threshold	Technician

Table 4-2. Laboratory Test Procedures Performed at Scripps Clinic

Chemistry	
2-hour Postprandial Glucose (mg/dl)	Gamma Glutamyl Transferase (GGT) (U/l)
Alanine Aminotransferase (ALT) (U/l)	Glycated Hemoglobin (percent)
Alkaline Phosphatase (U/l)	High Density Lipoprotein (HDL) Cholesterol (mg/dl)
Amylase (U/l)	Serum Creatinine (mg/dl)
Aspartate Aminotransferase (AST) (U/l)	Serum Insulin (µIU/ml @ 2 hours after fasting glucose)
Cholesterol (mg/dl)	Total Bilirubin (mg/dl)
Creatine Kinase (U/l)	Total Lactic Dehydrogenase (LDH) (U/l)
Direct Bilirubin (mg/dl)	Triglycerides (mg/dl)
Fasting Glucose (mg/dl)	
Coagulation	
Patient Prothrombin Time (seconds)	
Hematology	
Absolute Bands (thousand/mm^3)	Differential Segs (percent)
Absolute Basophils (thousand/mm^3)	Erythrocyte Sedimentation Rate (mm/hr)
Absolute Eosinophils (thousand/mm^3)	Hematocrit (percent)
Absolute Lymphocytes (thousand/mm^3)	Hemoglobin (gm/dl)
Absolute Monocytes (thousand/mm^3)	Mean Corpuscular Hemoglobin (MCH) (pg)
Absolute Reactive Lymphs (thousand/mm^3)	MCH Concentration (MCHC) (gm/dl)
Absolute Segs (thousand/mm^3)	Mean Corpuscular Volume (MCV) (cubic micra)
Differential Bands (percent)	Platelet Count (thousand/mm^3)
Differential Basophils (percent)	RBC Morphology
Differential Cells Counted	Red Blood Cell (RBC) Count (million/mm^3)
Differential Eosinophils (percent)	White Blood Cell (WBC) Count (thousand/mm^3)
Differential Lymphs (percent)	WBC Morphology
Differential Monocytes (percent)	Platelet Observation
Differential Reactive Lymphs (percent)	

Table 4-2. Laboratory Test Procedures Performed at Scripps Clinic (Continued)

Immunology	
Anti Delta Total Antibody	Hepatitis B Surface Antigen
Anti-Thyroid Antibody	Hepatitis B Surface Antigen Confirmatory
Hepatitis A Total Antibody	Hepatitis C Virus Antibody
Hepatitis B Core Antibody	
Lupus Panel	
Anti-Mitochondrial Antibody	Anti-Smooth Muscle Antibody
Anti-Nuclear Antibody	Latex Rheumatoid Factor (IU/ml)
Anti-Parietal Cell Antibody	Thyroid Microsomal Antibody
Fecal Studies	
Fecal Occult Blood	
Protein Profile	
α-1-Acid Glycoprotein (mg/dl)	Haptoglobin (mg/dl)
α-1-Antitrypsin (mg/dl)	IgA (mg/dl)
α-2-Macroglobulin (mg/dl)	IgG (mg/dl)
Albumin (mg/dl)	IgM (mg/dl)
Apolipoprotein B (mg/dl)	Prealbumin (mg/dl)
C3 Complement (mg/dl)	Transferrin (mg/dl)
C4 Complement (mg/dl)	
Radioimmunoassay	
Estradiol (pg/ml)	Prostate-Specific Antigen (ng/ml)
Follicle Stimulating Hormone (FSH) (mIU/ml)	T_4 (μg/dl)
Free Testosterone (pg/ml)	Thyroid Stimulating Hormone (TSH) (μIU/ml)
Luteinizing Hormone (mIU/ml)	Total Testosterone (ng/dl)
T & B Lymphocytes and Subsets (special immunology testing performed on 818 participants)	
CD20+ Cells (B cells) (percent)	Absolute CD16+56+ Cells (Natural Killer Cells) (per mm^3)
CD3+ Cells (T cells) (percent)	Absolute CD20+ Cells (B Cells) (per mm^3)
CD4+ Cells (Helper T Cells) (percent)	Absolute CD3+ Cells (T Cells) (per mm^3)
CD3+CD4+ Cells (Helper T Cells) (percent)	Absolute CD4+ Cells (Helper T Cells) (per mm^3)
CD8+ Cells (Suppressor T Cells) (percent)	Absolute CD3+CD4+ Cells (Helper T Cells) (per mm^3)
CD3+CD8+ Cells (Suppressor T Cells) (percent)	Absolute CD8+ Cells (Suppressor T Cells) (per mm^3)
CD45 Total Lymphs (Common Leukocyte Antigen) (percent)	Absolute CD3+CD8+ Cells (Suppressor T Cells) (per mm^3)
Lymphs (percent)	Absolute Lymphocytes (per mm^3)
	CD16+56+ Cells (Natural Killer Cells) (percent)
Urinalysis	
2-hour Postprandial Urine Glucose (g/dl)	Urinary Glucose (g/dl)
Leukocyte Esterase	Urinary Ketones (mg/dl)
Urinary Bacteria (per high-powered field)	Urinary Mucus (per high-powered field)
Urinary Bilirubin	Urinary Nitrites
Urinary Blood	Urinary pH
Urinary Casts (per low-powered field)	Urinary Protein (mg/dl)
Urinary Clarity	Urinary RBC (per high-powered field)
Urinary Color	Urinary WBC (per high-powered field)
Urinary Comment	Urine Specific Gravity
Urinary Crystals (per high-powered field)	Urobilinogen (Ehrlich unit/dl)
Urinary Epithelial Cells (per high-powered field)	

4.2 ADIPOSE TISSUE EXTRACTION

The follow-up results of the 1987 and 1992 Air Force Health Study (AFHS) showed a rise in the incidence of pre-diabetic indicators of type 2 diabetes, non-insulin-dependent diabetes mellitus (NIDDM), in the participants exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (dioxin). To examine the relation between dioxin exposure and glucose transporting activity in human adipose tissue cells, 313 participants volunteered to participate in a separate sub-study of the AFHS in which approximately 10 grams of adipose tissue were removed by liposuction and preserved for laboratory analysis. The information derived from the adipose tissue sub-study may help explain the positive association between dioxin body burden and diabetes mellitus in veterans of Operation Ranch Hand.

The Air Force designated 650 potential participants for adipose extraction by a random selection process within classifications of exposure, age, body fat, and diabetes. A consent form was provided to each adipose tissue-designated participant at the evening orientation. Over the course of the 1997 physical examination, a board-certified plastic surgeon extracted an adipose sample from 313 participants. The procedure lasted 30 minutes and required the use of a local anesthetic. The adipose tissue specimens were shipped to Brooks Air Force Base weekly for storage. The results of this study will be summarized in a separate report.

4.3 QUALITY CONTROL

As in the baseline and the 1985, 1987, and 1992 studies, quality control (QC) requirements for both laboratory testing and clinical procedures were extensive. Although details are provided in Chapter 6, the following categories summarize the extent of the emphasis on quality. For laboratory testing, Westgard rules (1_{2s}) were used throughout the study. Single reagent lots and control standards were used when practical, duplicate specimens were routinely and blindly retested, and testing overlaps were mandatory when test reagent lots were changed.

The Scripps clinical team was instructed to ensure clinician consistency. In total, 18 board-certified physicians in internal medicine, neurology, and dermatology participated in the general, specialty, and diagnostic examinations. In addition, 12 radiologists, 5 pulmonologists, and 4 cardiologists performed tests and interpreted results. To reduce observer variability, turnover in the clinical and paramedical staffs was minimized during the 11 months of examinations. One Scripps Clinic physician served as the Project Medical Director, responsible for the scheduling, conduct, and QC of the examinations. All examining physicians reviewed the mark-sense examination forms prior to a pre-examination test. To minimize recording errors, the layout of the form was designed to parallel the flow of the clinical examination. Because data transcription was not permitted, each physician was responsible for filling in the bubbled form. To a large extent, the use of these mark-sense forms and subsequent QC measures were the primary reason for a clean clinical data set. A complete set of forms is provided in Appendix B. Additional QC included the following elements:

- A detailed onsite quality control process was employed by Scripps Clinic, Science Applications International Corporation (SAIC), and Air Force physicians and personnel.
- Clinical quality assurance meetings were conducted to detect and correct problems.
- Examiners were unaware of the exposure status of the participants.
- Automated blood pressure recording was performed.

4.4 CONDUCT OF EXAMINATIONS

All examinations, from May 1997 to April 1998, were conducted in accordance with the Examiners' Handbook. Excluding weeks with national holidays, two groups of participants, averaging approximately 25 per group, were examined weekly.

A demanding logistics effort was required to contact, transport, and examine the 2,121 study participants. Pre-examination contact consisted of making telephone calls to recruit participants, determine special requirements (e.g., wheelchair assistance), and arrange transportation. Once scheduling was reasonably firm, the SAIC logistics coordinator sent each participant a detailed information package outlining dietary requirements, a stool occult blood testing kit (Hemoccult®), inbriefing schedules, important telephone numbers, a request for medical records, and local maps designating examination site dining and recreational facilities.

To encourage participation in future follow-up studies, some activities were continued in 1997. These included participant critique forms, an informational meeting open to any accompanying family members and friends, and preventive medicine examinations such as human immunodeficiency virus and prostate-specific antigen testing. Proctosigmoidoscopy, as well as treadmill tests, were made available to participants for a nominal fee. Accompanying family members also were offered the opportunity to use the clinic facilities at a discounted rate.

Each morning of the examinations, the current group of participants was transported to the Scripps Clinic, having fasted and abstained from nicotine and caffeine since midnight the previous evening. In addition, alcohol was strictly prohibited from 24 hours before the first day of the examination through the second day of the examination. On the first day, each participant was given an individualized 2-day schedule outlining his medical, interviewing, and laboratory appointments. The schedule carefully noted the specific required periods of caffeine and nicotine abstinence for generalized periods in relation to electrocardiograph testing. Although the clinic schedules generally were assigned at random, consideration was given to smokers and diabetics because of the fasting and abstinence restrictions. Figure 4-1 shows a typical 2-day schedule prepared for a participant. The participant depicted in this schedule was in good self-reported health, was a smoker, and was asked to participate in the blood measurement of dioxin on Day 2.

As in the previous examinations, schedules were printed with specific directions to aid participants in locating clinic departments, although for many tests, participants were escorted from the waiting room. Throughout the examination day, time was provided for waiting-room activities (i.e., renewal of past friendships, discussions of experiences in SEA, consumption of refreshments when permitted, and completion of paperwork). On the second day of the examination, the participants completed testing and examinations and received outbriefings from a medical diagnostician.

The psychological tests (the SCL-90-R and the Jenkins Activity Test) were self-administered and reviewed by a Scripps Clinic psychologist. If a problem was indicated, the participant was advised of the issue during his medical debrief. Upon completion of these debriefings, the participants were paid their stipend and reimbursed for travel expenses.

4.4.1 Blood Collection

On the first examination day, each participant had 160 ml of blood collected. Detailed immunology testing (see Table 4-2) was conducted on approximately 40 percent of the participants. These

AIR FORCE HEALTH STUDY

Participant Schedule for: Monday, May 05, 1997 and Tuesday, May 06, 1997

Case Number – group #

Participant's Full Name

Day: 1 Monday, May 05, 1997

Start Time	End Time				
0600		Meet in Hotel Lobby	Shuttle Bus	Transfer to Scripps	
0615		Bus to Scripps			
0630		Orientation and signing of consent forms	Green 2 N	Waiting Room	
0645	TBA*	Blood Draw 1 and 2	Green 2 W	Room W263 A	
0800		Physical Exam	AOP 3 A	Internal Medicine	Dr. Sargeant
0845		Dermatology	AOP 1 B	Dermatology	Dr. Cornell
1100		Chest X Ray	Green 1	Radiology	Please sign in
1200		Spirometry/ECG	Green 2 W	Room 264	
1300		Psychology Exam	Green 2 N	Room 231	
1415		Vibrotactile	AOP 3 A	Vascular Lab	Please sign in
1430		Doppler Exam	AOP 3 A	Internal Medicine	
1545		Bus to Hotel	Green 3 W	Outside Fountain	

TBA* = BLOOD DRAW 2 SCHEDULED 2 HOURS AFTER DRINKING GLUCOLA

NO FOOD, CAFFEINE, OR NICOTINE PRIOR TO BLOOD DRAWS 1 OR 2 ON DAY 1

NO CAFFEINE OR NICOTINE WITHIN 4 HOURS PRIOR TO DOPPLER EXAM, ECG, OR SPIROMETRY

MT01 smoker Good

Figure 4-1. Typical 2-Day Clinic Schedule

AIR FORCE HEALTH STUDY

Participant Schedule for: Monday, May 05, 1997 and Tuesday, May 06, 1997

Case Number – group #

Participant's Full Name

Day: 2 Tuesday, May 06, 1997

Start Time	End Time				
0615		Board Shuttle Bus	Hotel		
0630		Bus to Scripps			
0700		Blood Draw 3	Green 2 W	Room W263 A	
0800		Neurology Exam	AOP 3 A	Neurology – CHECK IN	Dr. Otis
0830		NORC Interview	Green 2 N	Room CP228	
1015		NIDR Dental Exam	Green 2 W	Room 213	
1315		Debriefing	AOP 3 A	Internal Medicine	Dr. Moore
1330		Exit Interview	Green 2 N	Waiting Room	Rita Taliaferro
1400		Bus to Hotel	Green 3 W	Outside Fountain	

TBA* = BLOOD DRAW 2 SCHEDULED 2 HOURS AFTER DRINKING GLUCOLA

NO FOOD, CAFFEINE, OR NICOTINE PRIOR TO BLOOD DRAWS 1 OR 2 ON DAY 1

NO CAFFEINE OR NICOTINE WITHIN 4 HOURS PRIOR TO DOPPLER EXAM, ECG, OR SPIROMETRY

MT01 smoker Good

Figure 4-1. Typical 2-Day Clinic Schedule (Continued)

participants were identified by the last digit of their participant study identification number used for previous testing, thus establishing a longitudinal connection between examinations. The immunologic tests were subjected to highly structured QC procedures set forth by the Air Force. Participants chosen for immunology testing had an additional 30 ml of blood collected. An additional blood collection of 10 ml was taken 2 hours after the first blood collection to assess 2-hour postprandial glucose and insulin. Blood bank chairs were used for maximum comfort and total body support in the event of a reaction. These chairs were selected because they could be shifted easily into the Trendelenburg position if a participant felt faint. Out of the 160 ml of blood collected from each participant, the Air Force was provided 40 cc of serum for archival purposes as well as human immunodeficiency virus and syphilis testing.

On the second day of the group examination, 563 participants were invited and provided a second blood collection for dioxin analysis at the Centers for Disease Control and Prevention. A total of 280 ml of blood was collected for these participants, unless the participant had blood collected for immunology testing the previous day. In this case, only 250 ml of blood was collected.

Table of Contents

List of Tables

List of Figures

5 STUDY SELECTION AND PARTICIPATION

5.1 INTRODUCTION

In this chapter, 1997 follow-up and cumulative study compliance are reviewed. Refusal rates are compared between Ranch Hands and Comparisons, as are the reasons for refusal. Reasons for refusal also are examined by age, race, and rank to detect any differences in refusal rates. All noncompliant Original Comparisons were to be replaced by Comparisons appropriately matched on age, race, rank, and self-reported health status. Adherence to the replacement strategy as defined in the study protocol (1) is assessed, and the health status of noncompliant Original Comparisons is compared to their Replacement Comparisons. Differences in the perception of health are evaluated by group, age, race, rank, and 1997 compliance status. Among fully compliant study participants, self-reported health status is compared. Because perception of health may differ between Ranch Hands and Comparisons, medication use and work loss are compared as possible surrogate measures of actual health status.

Throughout this chapter, several terms are used to describe veterans who did not participate in the 1997 examination. These terms include "passive refusal," "hostile refusal," and "final refusal." An individual who communicated a desire not to have any contact with or from the Air Force Health Study (AFHS) under any circumstances was classified as "hostile." Veterans who were classified as hostile in the past were not invited to the 1997 examinations (see Section 5.5.2.2). A veteran was classified as a "passive refusal" if he was scheduled for a physical examination but broke the appointment twice. He also could be classified as a passive refusal for other reasons, such as inability to contact him directly because of the presence of a "gatekeeper" (see Sections 5.5.2.1 and 5.5).

A veteran who was classified as hostile, or had refused to participate twice—passively or otherwise—was classified as a "final refusal." Prior to the second refusal, a "refusal conversion" attempt was made. The refusal conversion consisted of an attempt, made by a specially trained person, to convince the veteran to participate. If this conversion attempt failed, the veteran was classified as a final refusal.

5.2 FACTORS KNOWN OR SUSPECTED TO INFLUENCE STUDY PARTICIPATION

A multitude of factors may influence study participation. These may be broadly classified as health, logistics, demographic, operational, or publicity factors. For example, health factors are thought to include self-perception of health as well as demonstrable health indicators, such as medication use and work-days lost due to illness or injury. Logistics factors include distance to the examination site, reluctance to spend time away from family or job, income, and occupation. Demographic factors include flying status, age, race, or military duty status (active, retired, separated). Operational factors include any aspect of study operation that may cause differential compliance, such as differential treatment of participants during scheduling, physical examination, interview, or debriefing. Publicity factors are related to national attitudes and media presentations regarding the Agent Orange (Herbicide Orange) issue, the Vietnam War, veterans' health care, or health care in general. In addition, these considerations may influence Ranch Hands differently than Comparisons.

The decision to volunteer for this study is complex, making statistical assessment of compliance bias difficult and necessarily crude in that many of the factors contributing to self-selection cannot be measured directly. Instead, compliance bias was investigated at the 1997 follow-up with respect to self-perception of health, medication use, and work loss. Medication use and days lost from work due to

illness or injury were obtained from questionnaire and physical examination data and, therefore, were available only for fully compliant participants. In 1997, as in 1992, no partial compliance (defined as compliant to the questionnaire and noncompliant to the physical examination) occurred because both the physical examination and the questionnaire were administered at the examination site.

5.3 REPLACEMENT PROTOCOL

During the design phase of the AFHS, the authors of the study protocol anticipated that a loss of participants between follow-up examinations would pose the greatest threat to study validity. In particular, they expected differential compliance, with relatively more Ranch Hands choosing to return to the study than Comparisons and with health differences of unknown character between noncompliant Ranch Hands and noncompliant Comparisons. To partially correct the situation, the study design specified that noncompliant Comparisons would be replaced by Comparisons with the same values of the matching variables (age, race, and military occupation at the baseline examination) and the same health perception. Military occupation was stratified into the following five categories: (1) flying officer—pilot, (2) flying officer—non-pilot, (3) non-flying officer, (4) flying enlisted, and (5) non-flying enlisted (also referred to as enlisted groundcrew). In this way, the Replacement Comparisons would serve as surrogates for Comparisons who refused to participate. This method of replacement would tend to reduce bias resulting from refusal in the Comparison group and would maintain group size. No corresponding strategy for the Ranch Hands was possible because all living Ranch Hands had been identified and invited to participate.

The first Comparison in each randomized matched set who was asked to participate in the baseline questionnaire and physical examination was identified as the Original Comparison for his respective Ranch Hand (in accordance with the study protocol). If the Original Comparison was noncompliant, a "Replacement" Comparison was invited in his place. Noncompliance was determined if any of the following three conditions were met:

1. The Comparison refused to participate.
2. The Comparison was partially compliant (completed the baseline questionnaire but did not complete the baseline physical examination).
3. The Comparison was unlocatable.

Replacement Comparisons were identified as such in the database to satisfy the study protocol requirement that they be matched with the refusing Original Comparisons (also known as refusals) based on self-reported health (excellent, good, fair, or poor). Of course, in the case of an unlocatable Original Comparison, matching with regard to self-reported health was not possible. Original Comparisons who were partially compliant were replaced, but deceased Original Comparisons were not.

During the 1985 examination, a telephone questionnaire was administered to refusals and their potential replacements. This questionnaire served as the basis for health-matching required by the study protocol, and assessed self-perception of health, days lost from work due to illness, and medication use. Although the study protocol is not explicit on this point, it implies that the decision to include or exclude the replacements from the study should be based only on this health contrast. At the 1987 follow-up examination, instead of using a telephone questionnaire, refusals were asked during the scheduling process for their self-perception of health. During the 1992 and 1997 follow-up examinations, schedulers requested a current perception of health (compared to others their age) from all participants contacted by telephone. Health-matching of replacements was not used during the baseline examination but was implemented during the 1985, 1987, 1992, and 1997 follow-up examinations. Replacement Comparisons

were matched to noncompliant Original Comparisons with respect to age, race, rank, and military occupation at all examinations.

5.4 1997 FOLLOW-UP SCHEDULING AND REPLACEMENT OPERATION

5.4.1 Scheduling Strategy

The scheduling process included the following three objectives:

1. To maximize participation rates (in both the present and future follow-up studies)
2. To ensure that Ranch Hands and Comparisons were recruited using the same procedures and with the same effort
3. To ensure that, whenever possible, each Ranch Hand had at least one compliant Comparison who was matched with that Ranch Hand on age, race, and military occupation.

These objectives led to a set of conflicting priorities: maximizing participation rates meant giving each potential participant every opportunity and encouragement to participate, without being so persistent as to lose the cooperation of unwilling respondents in future follow-up examinations. This careful approach had to be balanced against the need to quickly identify noncompliant Comparisons. Until these noncompliant Comparisons were removed from the scheduling process, they could not be replaced. In general, prospective participants were contacted for scheduling in random order; however, priority was given to certain potential participants who needed to be contacted early in the scheduling period. These included the following:

- Veterans who live overseas, because they would be more difficult to contact and require more advance time to make travel arrangements
- Passive refusals or "no-shows" for previous physical examinations.

During the first 2 months of scheduling, an attempt was made to contact all veterans invited to previous examinations. In addition, all previously invited veterans were sent a refrigerator magnet that stated the date that scheduling would begin and the toll-free number of the scheduling operation.

Although every reasonable attempt was made to contact eligible veterans, accommodate unusual schedules, and convert refusals, experience in past examinations had shown that certain types of potential participants ultimately would not schedule appointments. To continue with the replacement of Comparisons, these cases needed to be closed early. Therefore, the following rules were observed to limit the number of calls to certain types of individuals who were not likely to participate:

- An individual classified as hostile to the study in previous follow-up examinations was not contacted in 1997.
- An individual who was extremely hostile in his refusal to initial scheduling contacts was coded as a final refusal with no refusal conversion attempts.
- If the scheduler did not get an answer on the telephone after eight attempts, a registered letter was sent to that individual. If there was direct evidence that the letter was received at the proper address and the individual did not respond to the registered letter, he was considered a passive refusal.
- An individual who broke two examination appointments ("passive refusal") was considered a final refusal.

- An individual who equivocated about attending the physical examinations twice during the first two contacts was considered a first refusal.
- One refusal conversion attempt was made for all first refusals.

Some potential participants were particularly difficult to reach because of the presence of a "gatekeeper" who did not allow the schedulers to speak directly to the potential participant. A potential participant was designated as a final passive refusal after a minimum of three contacts with a gatekeeper and failure to reach the participant by other means. These contact methods included varying calling times, leaving messages, or sending a certified letter. Up to eight gatekeeper contacts were allowed if the scheduling supervisor decided additional attempts were still warranted (e.g., if an individual had previously scheduled and canceled, if it seemed reasonable that he might reschedule). After these gatekeeper contacts had been exhausted, the individuals were designated as final passive refusals and, if eligible for replacement, replaced. Potential participants who were designated as final refusals at any stage in the scheduling process were provided with the toll-free number for the study and allowed to volunteer to participate at any time.

The percentage of persons completing the 1997 physical examination is plotted by calendar date in Figure 5-1 for Ranch Hands, Original Comparisons, Replacement Comparisons, and all Comparisons. These patterns are similar to those seen at previous follow-up examinations and reflect the study protocol specification that scheduling be random with respect to group. Completion rates are similar between Ranch Hands and Original Comparisons. Replacement Comparisons completed the physical examinations later in the scheduling process, as would be expected.

5.4.2 Replacement Strategy

All Comparisons who had been invited to participate in the baseline, 1985, 1987, or 1992 studies were invited to participate in the 1997 examination. If no previously invited Comparisons for a particular Ranch Hand agreed to participate in 1997, schedulers attempted to recruit a replacement. These replacements were selected from a set of up to 10 candidate Comparisons, matched by age, race, rank, and military occupation, whose self-reported health status in 1997 matched that of the noncompliant Original Comparison for a given Ranch Hand. Health status was recorded in four categories: excellent, good, fair, or poor. If a willing, health-matched participant was not found in the matched set, self-reported perceptions of health status were dichotomized into "excellent or good" and "fair or poor" categories, and these dichotomized health statuses were matched. If this second method for identifying a suitable replacement failed, no replacement was made.

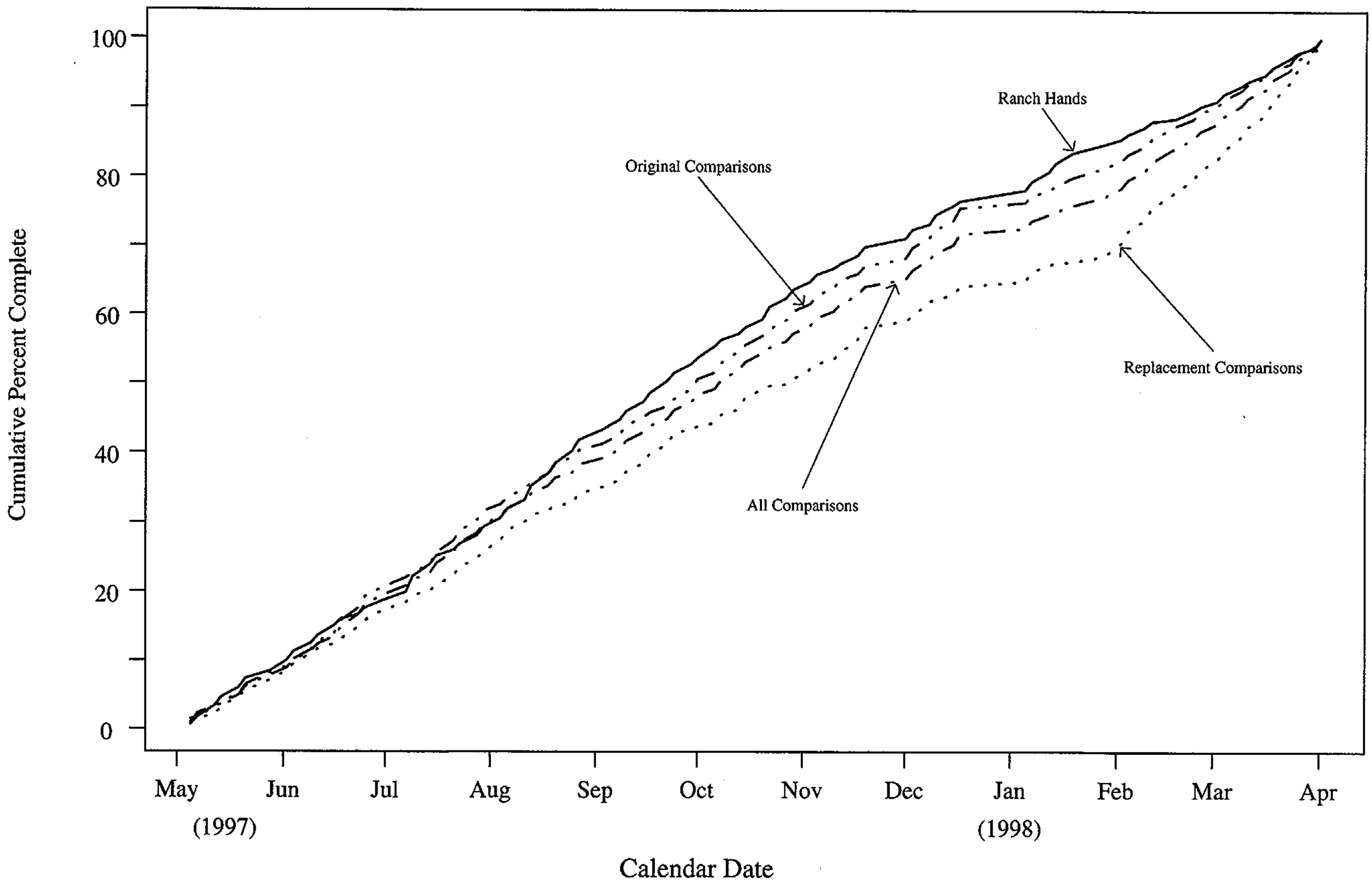

Figure 5-1. Cumulative Percent Completed Physical Examination by Calendar Date

There were two exceptions to the replacement strategy. First, the study protocol required that the noncompliant Original Comparisons report their health status during the scheduling effort so that they could be used to recruit Replacement Comparisons with the same health status. On occasion, Original Comparisons refused to speak with the scheduler or respond to questions. In these cases, a Replacement Comparison for the Original Comparison was recruited in the order in which he was listed in the randomized matched set. This strategy also was used for unlocatable and hostile Original Comparisons. Second, as specified in the study protocol, no replacement was made if all formerly invited Comparisons in a matched set were deceased.

5.5 COMPLIANCE

Of the 1,101 eligible Ranch Hands, 870 (79.0%) participated in the 1997 follow-up examination, while 839 (72.8%) of the 1,151 eligible Original Comparisons participated. Of the 768 Replacement Comparisons eligible for the 1997 follow-up, 412 (53.6%) chose to attend the examination. Table 5-1 provides compliance counts for Ranch Hands, all Comparisons as a group, and Original and Replacement Comparisons. Appendix C contains tables that describe these counts by compliance at the baseline examination. Table C-1 provides counts for the Ranch Hands. Total Comparison counts are summarized in Table C-2. Original Comparison counts are presented in Table C-3, and Replacement Comparison counts are provided in Table C-4.

In Table 5-1 and Appendix C, the "New to Study" rows include potential Replacement Comparisons who were found to be deceased when contact was attempted. The same deceased potential replacements are then accounted for in the rows marked "Died." Undefined categories are indicated by dashes. For example, in the Appendix C tables, dashes are shown when partially compliant participants at the baseline examination could not be partially compliant at a later examination. Partial compliance only occurred when a participant agreed to the baseline questionnaire but refused to attend the physical exam. As stated previously, no partial compliance occurred in 1992 or 1997 because both the baseline questionnaire and physical examination were given at the same site. As shown in Appendix C, Tables C-1 and C-2, 86 percent (819 of 949) of living Ranch Hands and 87 percent (976 of 1,116) of living Comparisons who were fully compliant at the baseline examination returned for the 1997 follow-up examination.

Table 5-2 describes the newly compliant participants in terms of their compliance at previous examinations. Two Ranch Hands, 9 Original Comparisons, and 69 Replacement Comparisons were fully compliant and examined for the first time at the 1997 follow-up examination. One Original Comparison and 52 Replacement Comparisons had not been invited previously to participate. The one Original Comparison who had not been invited previously to participate replaced an Original Comparison who was reclassified as a Ranch Hand (see Section 5.5.1). Two Ranch Hands, seven Original Comparisons, and five Replacement Comparisons had been previously invited and had refused to participate in one or more previous examinations.

Table 5-1. Compliance by Group and Examination Year

Time Period	Disposition	Group: Ranch Hands	All Comparisons	Original Comparisons	Replacement Comparisons
Baseline		***1,209***	***1,666***	***1,235***	***431***
1985 Examination	***Eligible***	***1,209***	***1,666***	***1,235***	***431***
Between Baseline & 1985 Examination	New to Study	9	73	17	56
	Died	(19)	(26)	(21)	(5)
	Remaining Eligible	***1,199***	***1,713***	***1,231***	***482***
	Subject Unlocatable	(39)	(65)	(48)	(17)
	Refused	(134)	(326)	(220)	(106)
	Partially Compliant	(9)	(30)	(9)	(21)
	Fully Compliant	***1,017***	***1,292***	***954***	***338***
1987 Examination	***Eligible***	***1,199***	***1,713***	***1,231***	***482***
Between 1985 & 1987 Examinations	New to Study	4	33	4	29
	Died	(15)	(16)	(13)	(3)
	Remaining Eligible	***1,188***	***1,730***	***1,222***	***508***
	Subject Unlocatable	(20)	(47)	(31)	(16)
	Refused	(171)	(358)	(242)	(116)
	Partially Compliant	(1)	(27)	(11)	(16)
	Fully Compliant	***996***	***1,298***	***938***	***360***
1992 Examination	***Eligible***	***1,188***	***1,730***	***1,222***	***508***
Between 1987 & 1992 Examinations	New to Study	(0)	83	2	81
	Died	(39)	(52)	(33)	(19)
	Remaining Eligible	***1,149***	***1,761***	***1,191***	***570***
	Subject Unlocatable	(12)	(56)	(15)	(41)
	No Health-Match	--	(11)	--	(11)
	Refused	(184)	(414)	(264)	(150)
	Fully Compliant	***953***	***1,280***	***912***	***368***
1997 Examination	***Eligible***	***1,149***	***1,761***	***1,191***	***570***
Between 1992 & 1997 Examinations	New to Study	(0)	236	2	234
	No Health-Match in 1992	--	(11)	--	(11)
	Died	(48)	(67)	(42)	(25)
	Remaining Eligible	***1,101***	***1,919***	***1,151***	***768***
	Subject Unlocatable	(4)	(29)	(10)	(19)
	No Health-Match	--	(91)	--	(91)
	Refused	(227)	(548)	(302)	(246)
	Fully Compliant	***870***	***1,251***	***839***	***412***

Table 5-2. Participants Newly Compliant in 1997 and Their Previous Compliance Pattern

Previous Compliance Pattern							
Baseline	1985	1987	1992	Ranch Hands	Original Comparisons	Replacement Comparisons	Grand Total
Partial	Refused	Refused	Refused	2	2	0	4
Partial	Refused	Unlocated	Refused	0	1	0	1
Partial	Refused	Unlocated	Unlocated	0	0	1	1
Partial	Unlocated	Unlocated	Refused	0	1	0	1
Partial	Unlocated	Unlocated	Unlocated	0	1	0	1
Refused	Partial	Refused	Refused	0	0	1	1
Refused	Refused	Refused	Refused	0	2	0	2
Refused	Refused	Refused	Unlocated	0	1	0	1
			Refused	0	0	3	3
			Unlocated	0	0	11	11
			No Health-Match	0	0	1	1
			New 1997	0	1	52	53
			Total	2	9	69	80

5.5.1 Corrections to Previously Reported Study Compliance Totals

Some changes were made to the historical cell counts shown in Table 5-1 (and the tables in Appendix C) so that they now differ from compliance tables presented during previous examinations (in particular, Tables 5-1 through 5-4 of the 1992 follow-up report). The differences are due to the following independent events:

1. One Original Comparison, who had been fully compliant since the baseline examination, was reclassified as a Ranch Hand. This participant was discovered to be part of stateside testing of Operation Ranch Hand and was assigned, on temporary duty, to the unit that transported Operation Ranch Hand equipment to SEA. This participant also was eligible as a Comparison because of a later assignment. The Ranch Hand assignment took precedence over the assignment as a Comparison. This change affects Tables 5-1, C-1, C-2, and C-3.
2. In the 1992 follow-up report, 3 Original Comparisons and 27 Replacement Comparisons who were new to the study since the baseline examination were classified as refusals for the 1985 follow-up examination. These numbers have been revised to indicate that 4 Original Comparisons and 26 Replacement Comparisons who were new to the study since the baseline examination were refusals at the 1985 follow-up examination. This change was due to the misclassification of one Original Comparison as a Replacement Comparison. This change affects Tables 5-1, C-3, and C-4.
3. In the 1992 follow-up report, two Original Comparisons and four Replacement Comparisons who were new to the study since the baseline examination were classified as partially compliant for the 1985 follow-up examination. These numbers have been revised to indicate that one Original Comparison and five Replacement Comparisons who were new to the study since the baseline examination were partially compliant for the 1985 follow-up examination. This change was due to the misclassification of one Replacement Comparison as an Original Comparison. This change affects Tables 5-1, C-3, and C-4.

4. In the 1992 follow-up report, 5 Original Comparisons and 28 Replacement Comparisons who were new to the study since the baseline examination were classified as new to the study between the 1985 and 1987 follow-up examinations. These numbers have been revised to indicate that 4 Original Comparisons and 29 Replacement Comparisons who were new to the study since the baseline examination were new to the study between the 1985 and 1987 follow-up examinations. This change was due to the misclassification of one Replacement Comparison as an Original Comparison. This change affects Tables 5-1, C-3, and C-4.

5. In the 1992 follow-up report, two Original Comparisons and five Replacement Comparisons who were new to the study since the baseline examination were classified as unlocatable at the 1987 follow-up examination. These numbers have been revised to indicate that one Original Comparison and six Replacement Comparisons who were new to the study since the baseline examination were unlocatable at the 1987 follow-up examination. This change was due to the misclassification of one Replacement Comparison as an Original Comparison. This change affects Tables 5-1, C-3, and C-4.

6. In the 1992 follow-up report, 4 Original Comparisons and 78 Replacement Comparisons who were new to the study since the baseline examination were classified as new to the study between the 1987 and 1992 follow-up examinations. In addition, three Replacement Comparisons who were new to the study since the baseline examination were classified as deceased between the 1987 and 1992 follow-up examinations. These numbers have been revised to indicate that 2 Original Comparisons and 81 Replacement Comparisons who were new to the study since the baseline examination were new to the study between the 1985 and 1987 follow-up examinations. In addition, the number of Replacement Comparisons who were new to the study since the baseline examination and classified as deceased between the 1987 and 1992 follow-up examinations has been revised from three to four. This change was due to the misclassification of two Replacement Comparisons as Original Comparisons and the addition of one deceased Replacement Comparison to the "New to Study" classification. This change affects Tables 5-1, C-2, C-3, and C-4.

7. In the 1992 follow-up report, 2 Original Comparisons and 27 Replacement Comparisons who were new to the study since the baseline examination were classified as unlocatable for the 1992 follow-up examination. These numbers have been revised to indicate that no Original Comparisons and 29 Replacement Comparisons who were new to the study since the baseline examination were unlocatable at the 1992 follow-up examination. This change was due to the misclassification of two Replacement Comparisons as Original Comparisons. This change affects Tables 5-1, C-3, and C-4.

8. In the 1992 follow-up report, 8 Original Comparisons and 44 Replacement Comparisons who were new to the study since the baseline examination were classified as refusals for the 1992 follow-up examination. These numbers have been revised to indicate that 6 Original Comparisons and 46 Replacement Comparisons who were new to the study since the baseline examination were refusals at the 1992 follow-up examination. This change was due to the misclassification of two Replacement Comparisons as Original Comparisons. This change affects Tables 5-1, C-3, and C-4.

5.5.2 Analysis of Refusals

Of the 1,101 Ranch Hands and 1,919 Comparisons eligible for the 1997 follow-up examination, 227 Ranch Hands and 548 Comparisons (302 Original and 246 Replacement) chose not to attend. Their reasons for refusal are summarized in Table 5-3. The 91 "no health-match" potential Replacement Comparisons included in Table 5-1 are not shown in Table 5-3. They also are not used in the analysis of refusals that follows because they were willing to participate but were excluded by the specifications of the study protocol.

Table 5-3. Reasons for Refusal by Group

	Group							
	Ranch Hands		Original Comparisons		Replacement Comparisons		Total	
Reason	n	%[a]	n	%[a]	n	%[a]	n	%[a]
Health Reasons	42	3.8	38	3.3	28	3.6	108	3.6
Job Commitment	33	3.0	49	4.3	55	7.2	137	4.5
No Time	26	2.4	35	3.0	39	5.1	100	3.3
Travel Distance, Family	14	1.3	21	1.8	21	2.7	56	1.9
Confidentiality	5	0.5	3	0.3	2	0.3	10	0.3
Financial Hardship	1	0.1	1	0.1	0	0.0	2	0.1
Passive Refusal	23	2.1	24	2.1	18	2.3	65	2.2
Hostile	55	5.0	96	8.3	49	6.4	200	6.6
Fear of Physical Exam	1	0.1	1	0.1	1	0.1	3	0.1
Dissatisfaction with USAF	1	0.1	6	0.5	0	0.0	7	0.2
Dissatisfaction with AFHS	3	0.3	4	0.3	4	0.5	11	0.4
Dissatisfaction with Previous Exam	5	0.5	5	0.4	1	0.1	11	0.4
Other	18	1.6	19	1.7	28	3.6	65	2.2
Total	227	20.6	302	26.2	246	32.0	775	25.7
Total Invited	1,101		1,151		768		3,020	

[a] Percent of persons invited.

Table 5-3 shows that a greater percentage of Comparisons than Ranch Hands refused, and a greater percentage of Replacement Comparisons than Original Comparisons refused (32.0% vs. 26.2%). Of the total invited, nearly the same percentages of Ranch Hands, Original Comparisons, and Replacement Comparisons refused due to health reasons (3.8%, 3.3%, and 3.6%, respectively). The percentages were also nearly the same for passive refusals (2.1%, 2.1%, and 2.3%, respectively). More Replacement Comparisons than Ranch Hands or Original Comparisons declined due to "job commitments" or "no time." More Original Comparisons were hostile refusals (8.3%) than either Replacement Comparisons (6.4%) or Ranch Hands (5.0%).

Table 5-4 summarizes reasons for refusal by group, age, rank, and race. Reasons for refusal have been collapsed to the following five categories:

1. Health (health reasons)
2. Logistics (job commitment, no time or interest, travel distance or family constraints, confidentiality, or financial hardship)
3. Passive (passive refusal)
4. Hostile (hostile refusal)
5. Other (fear of physical examination; dissatisfaction with the U.S. Air Force, U.S. Government, the AFHS, or previous examinations; or other reasons).

Table 5-4. Reasons for Refusal by Group, Age, Rank, and Race

		Reason for Refusal										
		Health		Logistics		Passive		Hostile		Other		
Category	Total Refusals	n	%	n	%	n	%	n	%	n	%	Unadjusted p-Value
Ranch Hand	227	42	18.5	79	34.8	23	10.1	55	24.2	28	12.3	0.092
Comparison	548	66	12.0	226	41.2	42	7.7	145	26.5	69	12.6	
Birth Year <1942	389	85	21.9	128	32.9	20	5.1	103	26.5	53	13.6	<0.001
Birth Year ≥1942	386	23	6.0	177	45.8	45	11.7	97	25.1	44	11.4	
Officer	248	29	11.7	81	32.7	18	7.3	94	37.9	26	10.5	<0.001
Enlisted	527	79	15.0	224	42.5	47	8.9	106	20.1	71	13.5	
Black	46	7	15.2	17	37.0	7	15.2	9	19.6	6	13.0	0.463
Non-Black	729	101	13.9	288	39.5	58	8.0	191	26.2	91	12.5	
Total	775	108		305		65		200		97		

Note: Percentages represent the percent of total refusals.

Age, rank, and race have been dichotomized for analysis purposes (born before 1942 and born in or after 1942; officer and enlisted; Black and non-Black, respectively). Without adjustment for age, rank, or race, the association between reason for refusal and group was not significant (p=0.092). There was a significant association between reason for refusal and age (p<0.001) and between reason for refusal and rank (p<0.001). Younger participants were less likely to refuse for health reasons than older participants (6.0% vs. 21.9%). Younger participants were more likely to refuse passively (11.7% vs. 5.1%) or for logistics reasons (45.8% vs. 32.9%). Officers were more likely to be hostile refusals than enlisted men (37.9% vs. 20.1%) and were less likely to refuse because of logistics reasons than enlisted men (32.7% vs. 42.5%). No significant association was found between reason for refusal and race (p=0.463).

A test of association between reason for refusal and group (adjusted for age, rank, and race) was performed and found to be not significant (p=0.132). The adjusted association between reason for refusal and age was significant (p<0.001), as was the association between reason for refusal and rank (p<0.001). No significant association was found for race (p=0.521).

5.5.2.1 *Passive Refusals*

A potential participant was classified as a passive refusal if he was scheduled for a physical examination but broke the appointment twice. A potential participant also was classified as a passive refusal for other reasons, including the inability to contact the participant directly because of the presence of a "gatekeeper" (see Section 5.5). Although passive refusal was the most common type of refusal (second only to hostile attitude) during the 1992 study, this type of refusal was far less prevalent in the 1997 follow-up. Passively refusing Ranch Hands, Original Comparisons, and Replacement Comparisons accounted for only 8.4 percent of the refusals (65 passive refusals, 775 total refusals) (see Table 5-3).

5.5.2.2 *Hostile Refusals*

Hostile refusals accounted for approximately 25 percent of both refusing Ranch Hands and refusing Comparisons. As shown in Table 5-5, 197 veterans were classified as hostile refusals during the 1992 physical examination process. Five additional veterans were added to the list of hostile individuals after the 1992 report was completed to bring the total to 202 individuals. Of these five, two were previously designated as refusals for the 1992 examination because of no interest in the AFHS, and three were dissatisfied with previous examinations. Between the 1992 and 1997 examinations, this list of 202 veterans was reviewed and some individuals were re-designated as refusals that should be contacted for the 1997 follow-up examination. Some hostile individuals on this list also contacted the Air Force and expressed a desire to participate in the 1997 follow-up examination. Consequently, 17 veterans were removed from the list of hostile individuals. Three of these previously hostile veterans participated in the 1997 follow-up examination, and the remaining 14 veterans refused to participate in the 1997 examination. Six additional veterans on the list of hostile individuals died between the 1992 and 1997 follow-up examinations. The list of 202 hostile individuals was therefore reduced to 179 veterans that were not to be contacted by schedulers for the 1997 examination. During the course of the 1992 examination, 21 additional veterans were designated as "newly" hostile individuals, resulting in a total of 200 veterans designated as hostile for the 1997 follow-up examination, as shown in Table 5-5.

5.5.2.3 *Reasons for Refusal Across AFHS Examinations*

The reasons for refusal for the baseline, 1987, 1992, and 1997 examinations are shown in Table 5-5, and are presented separately for Ranch Hands and Comparisons. The reasons for refusal to participate in the 1985 examination are not addressed in Table 5-5 because the data were not collected in a manner consistent with that in the other examinations. In 1985, the data were collected verbatim as part of the record of telephone contacts. Therefore, no meaningful comparisons can be made between the 1985 study data on refusals and other years. Table 5-5 shows a slight but consistent increase in total refusals across time. Of particular note is the steady increase in refusals for health reasons. Passive refusals decreased in the 1997 examination. This may be attributable to the aggressive efforts to maintain communication with veterans who were expected to become passive refusals.

Table 5-5. Reasons for Refusal by Group and Year

Reason	Baseline				1987				1992				1997			
	Ranch Hands		Comparisons		Ranch Hands		Comparisons		Ranch Hands		Comparisons		Ranch Hands		Comparisons	
	n	%[a]	n	%[a]	n	%[a]	n	%[a]	n	%[a]	n	%[a]	n	%[a]	n	%[a]
Fear of Physical Exam	6	0.5	6	0.4	1	0.0	4	0.2	0	0.0	3	0.2	1	0.1	2	0.1
Job Commitment	29	2.4	80	4.8	32	2.7	61	3.5	31	2.7	53	3.0	33	3.0	104	5.4
Dissatisfaction with USAF	5	0.4	0	0.0	10	0.8	11	0.6	6	0.5	10	0.6	1	0.1	6	0.3
No Time	53	4.4	154	9.3	28	2.4	79	4.6	13	1.1	50	2.8	26	2.4	74	3.9
Travel Distance, Family	4	0.3	21	1.3	5	0.4	17	1.0	8	0.7	17	1.0	14	1.3	42	2.2
Confidentiality	11	0.9	15	0.9	1	0.1	4	0.2	1	0.1	2	0.1	5	0.5	5	0.3
Health Reasons	10	0.8	7	0.4	11	0.9	16	0.9	19	1.7	21	1.2	42	3.8	66	3.4
Passive Refusal	9	0.7	15	0.9	40	3.4	78	4.5	41	3.6	96	5.5	23	2.1	42	2.2
Dissatisfaction with Previous Exam	n/a	0.0	n/a	0.0	0	0.0	1	0.1	3	0.3	5	0.3	5	0.5	6	0.3
Financial Hardship	n/a	0.0	n/a	0.0	1	0.1	1	0.1	2	0.2	2	0.1	1	0.1	1	0.1
Hostile	n/a	0.0	n/a	0.0	n/a	0.0	n/a	0.0	58	5.0	139	7.9	55	5.0	145	7.6
Dissatisfaction with AFHS	n/a	0.0	n/a	0.0	n/a	0.0	n/a	0.0	n/a	0.0	n/a	0.0	3	0.3	8	0.4
Other	0	0.0	3	0.2	42	3.5	88	5.1	2	0.2	16	0.9	18	1.6	47	2.4
Total	127		3010		171		360		184		414		227		548	
Total Invited	1,207		1,657		1,188		1,730		1,149		1,761		1,101		1,919	

[a] Percent of persons invited to participate.

5.5.3 Replacement Comparisons

As stated previously, matching replacements for refusing Original Comparisons based on health status, as well as age, race, rank, and occupation, was maintained at the 1997 follow-up. The reported health status of new replacements was obtained at the time of telephone scheduling. At the 1997 follow-up, 412 Replacement Comparisons were fully compliant (see Table 5-1). The health-matching results for the 52 Replacement Comparisons invited to the study for the first time in 1997 (see Table 5-2) and their replaced Original Comparisons are summarized in Table 5-6.

Table 5-6. Self-reported Health Status of Original Comparisons and Their Replacements

Replacement's Reported Health	Original Comparison's Reported Health					
	Excellent	Good	Fair	Poor	Unknown[a]	Total
Excellent	7	2	0	0	3	12
Good	2	22	0	0	6	30
Fair	0	0	3	1	4	8
Poor	0	0	0	0	0	0
Unknown	0	0	0	0	2	2
Total	9	24	3	1	15	52

[a] Includes 11 hostile respondents and 4 respondents who reported "Don't Know" for health status; one Replacement Comparison replaced a Replacement Comparison instead of an Original Comparison.

Thirty-two of the 52 Replacement Comparisons were matched perfectly on health status to the Original Comparisons. Five additional Replacement Comparisons were matched according to the dichotomized health status indicated in the study protocol. Fifteen Original Comparisons (labeled "Unknown") refused to give a self-perception of health or said they did not know how their health compared with that of others. The health status of these 15 Replacement Comparisons is shown in Table 5-6.

At the 1997 follow-up, 421 Original Comparisons were either deceased or noncompliant (see Table 5-7). The entire matched set of replacement candidates for each noncompliant Original Comparison was reviewed to determine if the appropriate replacement strategy was followed. Results are presented in Table 5-7. Of the 421 noncompliant (refusing, unlocatable, or deceased) Original Comparisons at the 1997 follow-up, 284 compliant replacements were found. Ninety-nine matched sets were closed because all previously invited Comparisons were deceased and, consistent with the protocol, no replacements were to be contacted, or because all replacements were contacted and no replacements were found that were willing to participate or were able to be health-matched. No Replacement Comparisons were contacted for 11 of the noncompliant Original Comparisons. A review of the record of telephone calls showed that all 11 had declined late in the scheduling process. For 27 of the noncompliant Original Comparisons, some replacements, but not all, were contacted and none complied. A review of the cohort of the 27 Original Comparisons, where replacement contact was not fully exhausted, showed that the Original Comparison or one or more of the Replacement Comparisons also had declined late in the process.

Table 5-7. Matched Set Compliance of Noncompliant Original Comparisons

Matched Set Compliance	Original Comparison's Compliance: Refusal	Unlocatable	Deceased	Total
At Least One Compliant Replacement	250	10	24	284
All Contacted Replacements Noncompliant and No Uncontacted Comparisons Remain in the Matched Set or All Previously Contacted Comparisons are Deceased	16	0	83	99
All Contacted Replacements Noncompliant and Other Uncontacted Comparisons Remain in the Matched Set	25	0	2	27
No Replacement Comparisons Contacted	11	0	0	11
Total	302	10	109	421

5.6 MATCHING OF SELF-REPORTED HEALTH STATUS

5.6.1 Self-reported Health Status of Refusals

Of the 775 refusals, reported health status, as obtained by telephone at the time of scheduling, was available for a total of 423 Ranch Hands and Comparisons. Table 5-8 summarizes their responses. Data were obtained from 125 (55.1%) of 227 refusing Ranch Hands and 298 (54.4%) of 548 refusing Comparisons. Among the 423 refusals responding to the health status question, there was no significant association between group and reported health (p=0.155).

Table 5-8. Reported Health Status of Refusals

Reported Health Status	Group: Ranch Hands n	Ranch Hands %	Comparisons n	Comparisons %	Total n	Total %	p-Value
Excellent	33	26.4	97	32.6	130	30.7	0.155
Good	64	51.2	152	51.0	216	51.1	
Fair	27	21.6	42	14.1	69	16.3	
Poor	1	0.8	7	2.3	8	1.9	
Total	125		298		423		

Note: Does not include 47 Ranch Hands and 107 Comparisons who reported "Don't Know" or refused to answer health status, and does not include 55 Ranch Hands and 143 Comparisons who were hostile.

Ideally, compliance bias between the groups should be assessed by comparing the health of refusing veterans to fully compliant participants with adjustment for the matching variables. The only current data available on the refusing veterans are self-reported responses to the health status question asked during the scheduling procedure. These data are missing for all hostile refusals. Almost three-quarters

(48 of 65, or 73.8%) of the passive refusals did not give their reported health status during scheduling. A summary of reported health status for 17 passive refusals that reported their health status during scheduling is shown in Table 5-9.

Table 5-9. Reported Health Status of Passive Refusals

Reported Health Status	Ranch Hands n	Ranch Hands %	Original Comparisons n	Original Comparisons %	Replacement Comparisons n	Replacement Comparisons %	Total	%
Excellent	0	0.0	1	25.0	1	20.0	2	11.8
Good	6	75.0	2	50.0	3	60.0	11	64.7
Fair	2	25.0	1	25.0	1	20.0	4	23.5
Poor	0	0.0	0	0.0	0	0.0	0	0.0
Total	8		4		5		17	

Note: Does not include 15 Ranch Hands, 20 Original Comparisons, and 13 Replacement Comparisons who reported "Don't Know" for health status.

A test of association between reported health status and group, age, rank, compliance, and race was performed, and the results are shown in Table 5-10. For analysis purposes, reported health status was classified into two categories: excellent or good, and fair or poor. The covariates age, rank, compliance, and race were dichotomized (born before 1942 and born in or after 1942; officer and enlisted; fully compliant and refusal; Black and non-Black, respectively). No significant association was found between race and reported health status (p=0.824). Without adjustment, age (p<0.001), rank (p<0.001), and compliance (p<0.001) were associated significantly with reported health. Ranch Hands were more likely to report fair or poor health than were Comparisons (14.1% vs. 11.1%). Enlisted men were more likely to report fair or poor health than were officers (15.1% vs. 7.6%). As expected, refusals (18.2%) and older participants (14.9%) were more likely to report fair or poor health than were fully compliant (11.0%) or younger participants (9.1%).

The association between reported health status and group, adjusted for age, rank, compliance, and race was significant (p=0.011). The adjusted association between reported health status and compliance was statistically significant (p<0.001), as were the adjusted associations between health status and age (p<0.001) and rank (p<0.001).

Table 5-11 shows the reported health status versus compliance separately by group. For both Ranch Hands and Comparisons, significantly more refusals reported fair or poor health (p=0.007 and p=0.001, respectively) than fully compliant participants. A higher percentage of compliant Ranch Hands reported fair or poor health (12.9%) than compliant Comparisons (9.7%). When adjusted for age, race, and occupation, the relation between health status and compliance did not change significantly with group (p=0.876). This result showed that the difference in health status between refusals and fully compliant participants was similar between Ranch Hands and Comparisons.

Table 5-10. Reported Health Status by Group, Age, Rank, Compliance, and Race

Group	Total	Reported Health Status				Unadjusted p-Value
		Excellent/Good		Fair/Poor		
		n	%	n	%	
Ranch Hand	963	827	85.9	136	14.1	0.028
Comparison	1,509	1,342	88.9	167	11.1	
Birth Year <1942	1,351	1,150	85.1	201	14.9	<0.001
Birth Year ≥1942	1,121	1,019	90.9	102	9.1	
Officer	935	864	92.4	71	7.6	<0.001
Enlisted	1,537	1,305	84.9	232	15.1	
Fully Compliant	2,049	1,823	89.0	226	11.0	<0.001
Refusal	423	346	81.8	77	18.2	
Black	144	125	86.8	19	13.2	0.824
Non-Black	2,328	2,044	87.8	284	12.2	
Total	2,472	2,169		303		

Table 5-11. Reported Health Status by Group

Group	Compliance Status	Total	Reported Health Status				p-Value
			Excellent/Good		Fair/Poor		
			n	%	n	%	
Ranch Hand	Fully Compliant	838	730	87.1	108	12.9	0.007
	Refusal	125	97	77.6	28	22.4	
Comparison	Fully Compliant	1,211	1,093	90.3	118	9.7	<0.001
	Refusal	298	249	83.6	49	16.4	

5.6.2 Self-reported Health Status of Fully Compliant Participants

Tables 5-12 through 5-14 summarize the reported health status, medication use, and work loss of the 2,121 fully compliant participants at the 1997 follow-up examination. Table 5-12 summarizes the reported health status of participants fully compliant to the 1997 physical examination. Among fully compliant participants, a marginally significant association was found between reported health at the time of scheduling and group (Ranch Hand, Comparison) (p=0.076). More Ranch Hands reported their health as fair (12.9%) than did Comparisons (9.7%).

Table 5-12. Reported Health Status of Fully Compliant Participants

Reported Health Status	Group						
	Ranch Hands		Comparisons				
	n[a]	%	n[a]	%	Total	%	p-Value
Excellent	287	34.2	440	36.3	727	35.5	0.076
Good	443	52.9	653	53.9	1,096	53.5	
Fair	108	12.9	118	9.7	226	11.0	
Poor	0	0.0	0	0.0	0	0.0	
Total	838		1,211		2,049		

[a] Does not include 32 Ranch Hands and 40 Comparisons who answered "Don't Know."

Table 5-13. Reported Medication Use of Fully Compliant Participants

Medication Use	Group						
	Ranch Hands		Comparisons				
	n[a]	%	n	%	Total	%	p-Value
Yes	512	58.9	688	55.0	1,200	56.6	0.081
No	357	41.1	563	45.0	920	43.4	
Total	869		1,251		2,120		

[a] One Ranch Hand did not report on medication use.

Table 5-14. Reported Work Loss of Fully Compliant Participants

Work Loss	Group						
	Ranch Hands		Comparisons				
	n	%	n	%	Total	%	p-Value
Yes	105	16.7	148	16.5	253	16.6	0.968
No	524	83.3	750	83.5	1,274	83.4	
Total	629		898		1,527		

Note: Does not include the following: 22 unemployed (9 Ranch Hands, 13 Comparisons)
564 retired (231 Ranch Hands, 333 Comparisons)
8 who did not answer (1 Ranch Hand, 7 Comparisons).

A marginally significant association was found between reported use of medication and group (p=0.081). As shown in Table 5-13, a greater percentage of Ranch Hands (58.9%) reported medication use than did Comparisons (55.0%). Use of medication increased in both groups since 1992; however, that increase was parallel. In 1992, 44.1 percent of Ranch Hands and 40.4 percent of Comparisons reported medication use compared to 58.9 percent and 55.0 percent, respectively, in 1997. Table 5-14 shows reported work loss for fully compliant Ranch Hands and Comparisons. The difference between the two groups narrowed from 1992, and no significant association was found between work loss and group (p=0.968) in 1997.

5.7 CONCLUSION

Although more Comparisons than Ranch Hands refused to participate in the 1997 follow-up examination, there is no significant difference in the reasons for refusal among the two groups. The reasons for refusal differed with age and rank but did not differ significantly for race. Logistics and health reasons were the most common reasons for refusal, although there were a substantial number of veterans deemed hostile from whom a reason for refusal was not determined. In replacing noncompliant Original Comparisons, either compliant replacements were found or no replacement was necessary (e.g., the Original Comparison was deceased and no Replacement Comparison had been contacted previously) for approximately 91 percent of the cases.

Self-reported health status differed with group, age, rank, and compliance status, but not with race, among those reporting health status. Ranch Hands, older participants, enlisted men, and refusals were more likely to report fair or poor health. Ranch Hands reported fair or poor health more often than did Comparisons. In both groups veterans who refused were more likely to report fair or poor health than those who were fully compliant. This pattern of Ranch Hands reporting poorer health has been observed since the baseline examination. Using work loss and medication use as more objective indicators of health than health perception, Ranch Hands reported a slightly higher use of medications, but no difference was seen in reported work loss between Ranch Hands and Comparisons. A further analysis of self-perception of health, as reported by fully compliant participants at the 1997 follow-up examination, is given in Chapter 9, General Health Assessment.

In summary, the results of these analyses suggested that Ranch Hands may be reporting poorer health than Comparisons and that these group differences are present for both fully compliant participants and refusals. This holds true even after accounting for rank and age differences. In addition, the difference in the percentage of fully compliant participants and refusals reporting fair or poor health was similar for Ranch Hands and Comparisons.

REFERENCE

1. Lathrop, G. D., W. H. Wolfe, R. A. Albanese, and P. M. Moynahan. 1982. Epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Study protocol. NTIS: AD A 122 250. USAF School of Aerospace Medicine, Brooks Air Force Base, Texas.

Table of Contents

List of Figures

6 QUALITY CONTROL

Quality control (QC) and quality assurance (QA) procedures were planned for and implemented throughout the 1997 Air Force Health Study (AFHS), from project initiation to final product delivery and acceptance by the Air Force. QC is defined as the procedures put in place to ensure the quality of the data collected. QA refers to the management of those procedures. This chapter provides an overview of the specific QC and QA measures developed and used by the project team, specifically in the areas of questionnaire and physical examination QC, laboratory QC measures, data management QC, statistical QC, and administrative QA. The Air Force, Science Applications International Corporation (SAIC), the National Opinion Research Center (NORC), and Scripps Clinic all participated in the formulation and implementation of the QC and QA procedures described in this chapter.

6.1 QUESTIONNAIRE QC

6.1.1 Design

For the baseline and subsequent follow-up examinations, the baseline and interval questionnaires were administered in person. In the examinations prior to 1997, the questionnaires were administered in hard copy, which was then key-entered into the final SAS®[1] data set. For the 1997 follow-up, the interview responses were obtained electronically on laptop computers, using a computer-assisted personal interview (CAPI) system.

Effective CAPI design was the first step in QC of the data collection. By combining the two steps of data collection and data entry, the CAPI technique eliminated one possible source of recording error—key-entry of the data. Further, the logic checks, range checks, and intervariable consistency checks programmed into the CAPI system placed constraints on what the interviewer could type or select for any particular question during the interview. These constraints limited keystroke errors and data problems arising from the interview itself. The structure of the CAPI system ensured that skip patterns were followed correctly and that no questions were left unanswered. In certain sections of the questionnaire, CAPI offered significant enhancements to the flow and accuracy of the questionnaire over a paper-and-pencil execution. These enhancements included automatic unit conversions and elimination of multiform cross-references. These benefits were most notable in the calculations of alcohol and tobacco use and in updating information for children born prior to the last interview.

Using a process of reviewing, commenting, and concurring, Air Force researchers and NORC designers incorporated new questions and questions derived from the AFHS self-administered forms into the 1997 questionnaire. The goal was to create a cohesive instrument with questions grouped logically by subject because a cohesive questionnaire would enhance the participant's focus on the subject being discussed and his understanding of the questions. In addition, the inclusion of the self-administered forms into the interval questionnaire decreased the participants' frustrations with the study process by eliminating question redundancy, providing a logical sequencing of questions, and decreasing the time spent by the participant.

[1] SAS and all other SAS Institute, Inc., product and service names are registered trademarks or trademarks of SAS Institute, Inc., in the USA and other countries.

An additional benefit of the CAPI questionnaire was the ability to print selected participant responses for the use of the debriefing physicians. These printouts were improved and refined during the physical examination period.

6.1.2 Data Collection

NORC recruited and trained eight interviewers and one field manager to administer the baseline and interval questionnaires. A minimum number of interviewers were selected to reduce variability between interviewing techniques. The interviewers were blind to the participants' exposure status, thus avoiding bias.

The Field Manager, who supervised the interviewing at the examination site, observed the work of each interviewer and presented formal evaluations of their performance each quarter to the Air Force. Interviewers were evaluated on their ability to control the interview and to probe incomplete answers in a neutral manner. They also were graded on their vocal quality, reading quality, and on their use of associated forms and documents. The interviewers were graded on a scale of 1 to 4. A rating of 1 indicated an unacceptable performance and 4 an above-average performance with no errors. All interviewers performed at an above-average level and none required retraining.

Interviewers were required to regularly report questions or problems experienced while executing the questionnaires. "CAPI Problem Forms" and "Policy Decision Forms" were distributed for interviewers to complete, and these forms were faxed daily to the Data Collection Task Leader at NORC headquarters in Chicago, Illinois. Items reported on the forms included the following: (1) mistakes made and not corrected during the interview, (2) conditions reported by the participant after the interview was over, (3) technical problems with the CAPI instrument, and (4) problems with the printout for the debriefing physician. The Data Collection Task Leader corrected problems when necessary and provided assistance to interviewers in handling confusing or unusual situations.

6.1.3 Processing and QA of Questionnaire Data

Completed questionnaire data were transmitted daily via modem from the La Jolla, California, site to the receiving computer system in Chicago. As interviews were completed on the laptop computers at the site office, the CAPI system selected the newly completed cases, encrypted the interview data, and transmitted the interview data to the NORC modem pool in Chicago. Once in Chicago, the interview data were unencrypted, archived on a devoted volume of the NORC UNIX computer, and copied to the NORC wide area network. Each CAPI interview consisted of one multiple-record ASCII file representing the participant's answers to questions. Using a standard utility, the ASCII files were converted from their vertical format to the horizontal format readable by SAS®. Programmers then read the horizontal files into SAS® and printed frequencies of all variables. Case data received in Chicago were reconciled regularly with the completion log at the interviewing site.

Some of the QC steps used in converting CAPI files to the SAS® data files include the following:

1. The case IDs of all completed interviews in the SAS® file were compared to the log of completed interviews kept at the site office. This ensured that all completed cases were received and that there were no duplicates.
2. The SAS® variables were compared to a hard-copy representation of the CAPI to ensure that all questions in the interview were present in the SAS® data file.

3. The response frequencies were compared to a hard-copy representation of the CAPI to ensure that no data were truncated.

One of the goals in the conversion process was to replicate, to the maximum extent possible, the variable names, formats, and structures used in the 1992 SAS® data set. To accommodate this goal, additional "post-processing" programs were created. The post-processing included renaming variables, assigning the appropriate variable labels and value labels, creating variables based on values of answers to more than one question (such as calculations of cigarette use), and merging variables collected outside of the interview into the data set.

Several steps were taken to ensure that the SAS® data file created from the post-processing programs contained the correct information:

- A list was created that mapped CAPI variables to SAS® variables. This allowed the NORC staff to ensure that variables were named properly and that all required variables were included in the SAS® data set.
- Format statements and frequencies were proofed against three representations of the questionnaire (the CAPI form, the 1997 hard copy representation, and the 1992 hard copy) to detect problems.
- Cross-tabulations and printouts of data items at the case level were generated to investigate complicated questions, such as whether a calculation was working correctly or why there was a missing value in a certain variable.
- Continuous reviews of the frequencies were performed until no more errors were detected.
- A cumulative data set of all interviews completed to date, accompanied by a footnote file explaining any anomalies or errors still to be resolved, was delivered quarterly and then monthly to the Air Force for review. All errors identified by the Air Force were corrected by NORC, the data set was corrected and delivered a final time, and the corrections were accepted.

Response frequencies for all data fields were reviewed regularly to ensure that data for all variables were captured, answers made logical sense, and the skips and checks programmed by CAPI were operating correctly. These QC checks revealed a small number of problems in the questionnaire, all of which were corrected without significant loss of data. These problems, along with the solutions applied, were documented in the footnotes included with the data file.

One of these problems was discovered during processing of the first questionnaires. During a variable-by-variable review of the interval questionnaire, NORC discovered that a short series of questions concerning mental and emotional illness had been omitted from the CAPI program. Three steps were taken to correct this situation:

1. A hard-copy version of the questions was immediately distributed to NORC's interviewers at Scripps Clinic so that the information would be obtained for the remaining participants in the current physical examination group. These data were manually entered into the questionnaire database.
2. A revised version of the interval questionnaire, containing the omitted questions, was installed on the interviewers' computers within 6 calendar days of the problem discovery.

3. NORC schedulers telephoned the participants who were not asked the omitted questions during their in-person interview to retrieve the information. These data were manually entered into the questionnaire database.

6.2 PHYSICAL EXAMINATION QC

The Scripps Clinic selection process for all personnel who were to interact directly with the participants ensured a high-quality physical examination. Each staff member was hand-selected for the AFHS on the basis of expertise, experience, and a commitment to remain with the study throughout the examination process. Further, the Air Force reviewed the credentials of all key staff members and approved their participation in the study.

A complete pre-examination test was held. Eleven volunteers completed the physical examinations, interviews, psychological tests, and laboratory analyses several weeks before the scheduled start of the study. All aspects of patient contact were reviewed: the initial inbriefing of the participants, the logistics of transportation and patient flow within the clinic, and the final outbriefing by the diagnostician.

During the actual examinations, refinements were made whenever operational problems were detected. Whether detected by the Scripps staff, the Air Force onsite monitor, or the participants, study problems were addressed during periodic clinical QA meetings of key Scripps staff. For instance, participant temperatures were not recorded for the first few physical examination groups. This error in protocol was addressed in one of these meetings. The Air Force reviewed the affected records, found no comments concerning elevated temperatures, and coded these records as normal.

During the physical examination, the identification of 27 chest x rays was found to be questionable because of incomplete or improper labeling. Although no data from the x rays were to be used in the analysis, the 27 participants whose x rays were in question were contacted and arrangements were made to reshoot their x rays. All but six x rays were retaken; two participants refused.

Following examination of each participant group, the Scripps staff reviewed all physical examination forms for omissions, incomplete examinations, and inconsistencies. When issues were found, the examiners or technicians were contacted to correct the data. Special effort was made to complete this review while the participants were at the examination site. In all cases in which data were corrected, the form was initialed by the doctor or technician making the correction. (This subject is discussed in more detail in the Medical Data QC section of this chapter.) An optical scanner read all mark-sense physical examination forms as an ongoing QA of form completion.

The Air Force onsite monitor and the Scripps Clinic administrative team monitored compliance with the physical examination process. The Scripps Clinic Chief of Medicine and the SAIC Project Manager conducted additional periodic inspections. All such clinical reviews were performed unobtrusively and with the full consent of the participant; suggestions or corrections to the examination procedure always were discussed privately with the attending physician. These inspections emphasized aspects of clinical techniques, sequence, and completeness of the clinical data with respect to the examination forms and the blindness of the examinations. Of particular note were the detailed daily log entries of the Air Force monitors. These entries ensured continuity of knowledge (the monitors rotated approximately every 2 weeks) by documenting daily activities and, when needed, recording events requiring follow-up by either the Air Force or SAIC.

Establishing a rapport with each study participant was a primary goal of all the organizations involved in the study. Although this may not be a traditional QA parameter in most research studies, it is paramount in the AFHS. Maintaining participants' satisfaction encourages them to continue in the study, thus avoiding the need for significant participant replacement, which can reduce future statistical power or introduce bias, or both. Therefore, every staff member emphasized courtesy, empathy, assistance, and personalized treatment of each participant.

Participants were asked to fill out an evaluation form after completion of their 1997 follow-up physical examinations. The participant evaluations provided insight into the participants' experiences, including strong points of the programs and areas in need of improvement. These forms were reviewed by all study management staff.

Based on the participants' evaluation forms, 72.8 percent evaluated their overall clinic experience as excellent, and 25.0 percent classified it as good. One participant felt that the experience was unsatisfactory, and 2.1 percent of the participants rated it as satisfactory. Figure 6-1 charts those evaluations of the participants' clinic experiences.

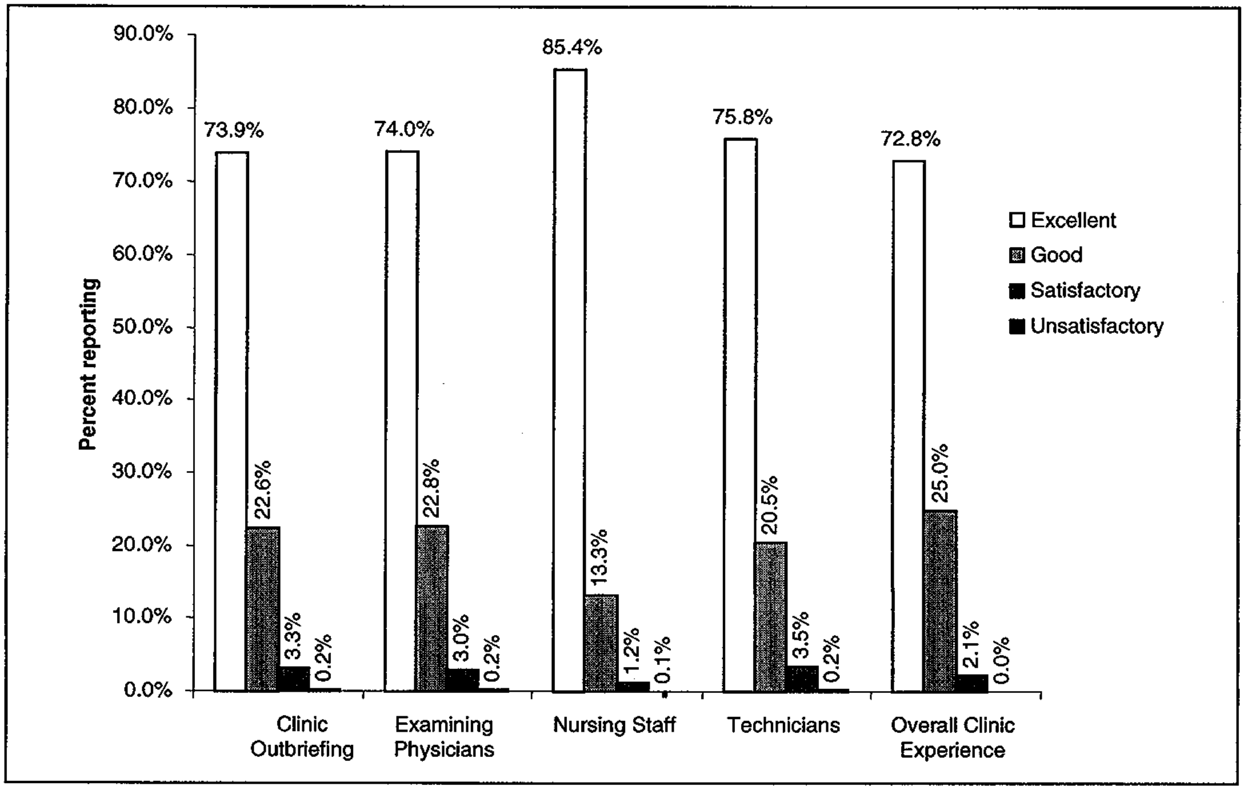

Figure 6-1. Participant Evaluations of the 1997 AFHS Clinic Experience

6.3 LABORATORY QC

Before the study began, specific QC laboratory procedures were designed, developed, and implemented to detect problems related to test and assay performance, validity of reagents, analysis of data, and reporting of results. All laboratory assays for the study were performed with state-of-the-art laboratory equipment and techniques. Laboratory facilities all had the equivalent of National Institutes of Health Biosafety Level 2 approval ratings and were certified by the College of American Pathology.

6.3.1 QC Procedures for the Clinical Laboratory

The following list outlines the tests performed and the methods and equipment used:

- Hematology assays were performed on Coulter STKS® equipment.
- Erythrocyte sedimentation rate determinations were performed using the large-tube Westergren method.
- Biochemical assays were performed using the Dade RxL® Automated Chemical Analyzer.
- Radioimmunoassays were performed with standard test kits.
- Electrophoresis and occult blood tests were performed manually.
- Hepatitis A, B, C, and D tests were performed using Abbott Commander® and Quantum® machines.
- Monospecific antibodies were used for immunoglobulin assays using the Beckman Array Protein System®.
- T & B lymphocytes were analyzed on BD FACSCAN equipment.
- Blood-cell counts were performed with standard microscopy.
- All urinalyses were performed using Bayer Atlas® equipment.
- All other assays were performed using industry-standard equipment and techniques.

All laboratory operations were controlled with the use of an integrated medical laboratory management information system that incorporated direct device-to-database interfaces for automated testing equipment. Laboratory technologists performed data entry for manual tests. An automated audit trail and a set of comments for technologist remarks were kept for each test so that any QC results could be retraced.

Procedural QC included using the same instrument and reagents from the same lot numbers whenever possible throughout the study. If single lots were unavailable, analyses were conducted to calibrate subsequent lots and establish target levels and associated standard deviations. Strict standards of calibration for all automated laboratory equipment were maintained at all times.

Trilevel or bilevel controls were used as the primary means for monitoring the quality of all tests. On every group of participant samples, one control (low, medium, or high) was run at the start, after every ninth sample, and at the end of each test run. Each trilevel control was used before repeating it in the run when more than 18 experimental samples were analyzed. In addition, split aliquots were created from every 10th participant sample and were analyzed separately to measure test reproducibility. In radioimmunoassays, all three control levels were run initially to validate the standard curve generated.

Scripps Clinic Medical Laboratory has defined quality requirements of accuracy above 99 percent and levels of precision above 97 percent. A variation of the Westgard Rules (1, 2) QC technique is routinely used in the Scripps Laboratory and was used for AFHS assays. In this variation, the 1_{2s} single rule and 4_{1s} multiple rule are used. The 1_{2s} rule indicates rejection of any run when the control value of any one of the three controls (low, mid, high) exceeds two standard deviations from the mean. The 4_{1s} rule indicates rejection of a run when four consecutive control measurements exceed one standard deviation on the same side. This approach ensures an effective system for reducing the probability of false rejection to the lowest acceptable level while maintaining error detection at more than 98 percent.

All QC data were analyzed and summarized in formal QC reports generated monthly. QC data were subjected to independent statistical analysis by the Air Force to produce and analyze time-dependent trends. For all equipment malfunctions or other exceptions, a formal QC exception report was prepared by the responsible individual and forwarded to the project management team. A summary of the coefficients of variation for each quantitative laboratory assay is presented in Appendix D. These coefficients of variation are given separately for each control level and lot.

As the examination portion of this study ended, an independent clinician analyzed laboratory outliers for logical validity. All out-of-range test results were examined and scored as "clinically explainable," "clinically possible," or "clinically unexplained." No clinical laboratory data were excluded from the report analyses because all potential out-of-range results were found to be clinically explainable or clinically possible.

6.4 MEDICAL DATA QC

6.4.1 Overview of QC Procedures

The QC procedures for the medical data consisted of multiple checks at all stages of the examination, data collection, and data processing cycle. A representation of the QC process is given in Figure 6-2. Although improvements were made throughout the physical examination period, QC procedures for data collection, conversion, and integration were developed before the clinical examinations began. All data collection instruments were tested at the pre-examination test conducted several weeks before the start of participant physical examinations. In addition, during the first 2 months of the clinical examinations, all data collection activities were routinely scrutinized to detect and correct procedural deficiencies. Other QC activities included the following:

- Automated QC techniques applied to laboratory data
- Clinical evaluations of all laboratory outliers
- Review of all physical examination findings by one of two diagnosticians
- Automated and manual data quality checking of hard copy against transcribed computer files.

Four interwoven layers of QC were instituted to ensure data integrity. These efforts focused on (1) data processing system design, (2) design and administration of all exams, (3) data completeness checks, and (4) data validation. In addition, Air Force investigators reviewed all physical examination forms and entries. Forms that were found to be questionable, inaccurate, or incorrect were returned to Scripps Clinic for adjudication.

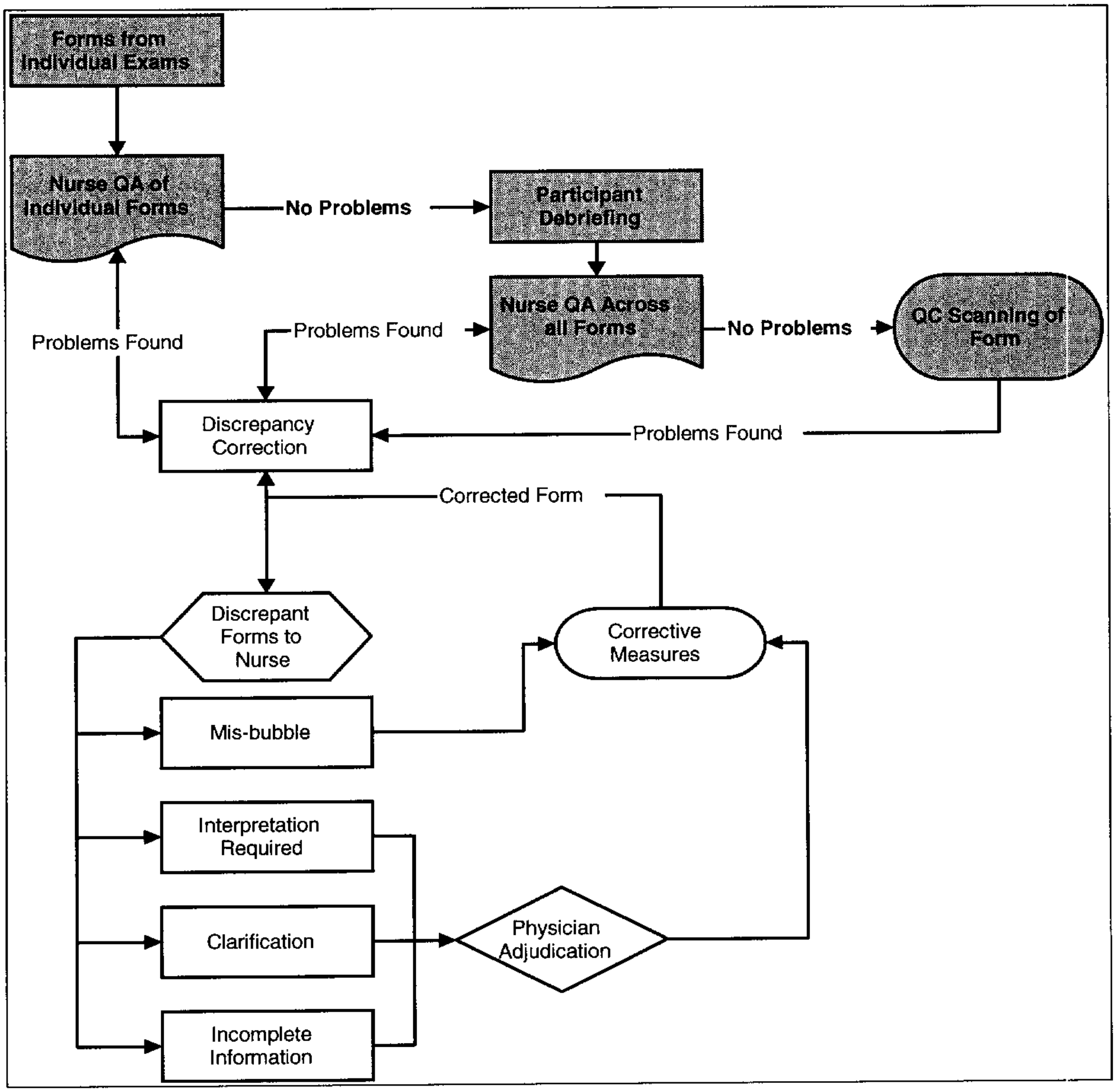

Figure 6-2. Physical Examination Form QC Process

6.4.2 Data Processing System Design

Standards were established for data element formats (character or numeric), data element naming conventions, data element text labels, numeric codes for qualitative responses and results, QC range checks for continuous data elements, and QC validity checks for categorical data. A data dictionary provided detailed information on each data element.

A systems integration approach was applied to the design and implementation of data collection procedures so that data emanating from study sources (physical examination, questionnaire, and laboratory) were consistent in file format and structure. This approach was necessary to ensure that all data could be integrated into a single database for analysis.

Data collection forms were carefully designed to ensure that all required data elements would be collected in accordance with the study protocol and in a standardized format. These instruments were designed to reflect the order in which the examination itself would be administered and to provide for the sequential coding of information.

Completed clinical examination forms were converted from hard copy to machine-readable images using optical mark reading equipment. Verification procedures were performed to ensure that a uniquely identified participant record existed within each data file and that the appropriate number of responses for each applicable field was provided. Data files were then translated into a SAS® data set, verified against original data sheets, and corrected as necessary. All corrections to the original data sets were saved in the processing program, which was delivered to the Air Force for verification.

Next, the SAS® data sets were subjected to validity checks. All potentially conflicting results, as well as any data values falling at the extremes of expected ranges, were manually reviewed. Extreme values were verified against the original data forms and either corrected or documented as valid results. Potentially conflicting results, either within one form or among forms, were returned to the examiners for review. These results were then documented as having been correctly recorded, corrected, or flagged for exclusion from analysis because of unresolvable examiner errors or omissions. This process was continued until all results were properly documented.

The validity checks were tested with the delivery of the first cumulative medical results data. At that time, it was discovered that some data were not properly cross-checked between collection forms. The discrepancies were adjudicated by the appropriate Scripps Clinic staff and corrected on the forms and in the database in accordance with the QC procedure. Additional QC steps were added to the procedures because of these discrepancies.

Once the edits were completed and the data verified, the "cleaned" files were transferred to the data analysis center for final inspection and integration into the study database. In this QC measure, descriptive analyses were run. The validation, correction, transmission, and analysis QC procedures were repeated as necessary to ensure that all extreme or suspicious values had been validated. As an additional measure of QC, cumulative result data sets were delivered quarterly during the physical examination phase for Air Force review. The data sets were finalized following the close of the physical examinations and before the start of statistical analysis. The process for cleaning and converting the collected data into final data sets is found in Figure 6-3.

6.4.3 Design and Administration of Physical and Psychological Examination Forms

The examination forms were designed to elicit all required data while minimizing recording time, enhancing comprehension, and automating data input. Customized mark-sense forms were developed and optical mark recognition technology (OMR) was used to eliminate the risk of transcription errors. The use of mark-sense forms allowed the creation of computerized data files directly from the raw data recorded on these forms.

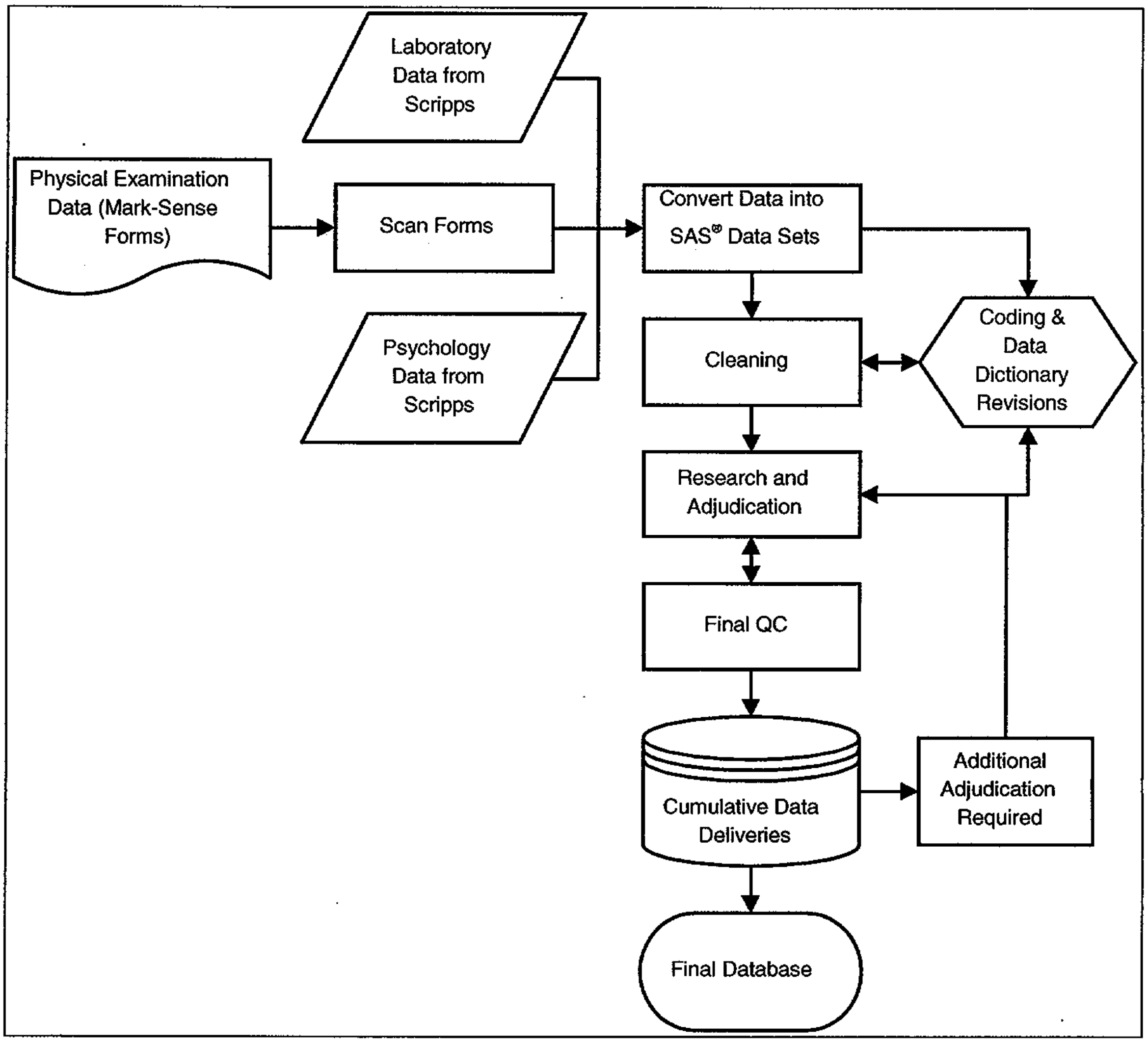

Figure 6-3. Conversion and Cleaning Process for Medical Data

QC procedures for all data collection instruments began with both manual and electronic reviews of each form as it was completed. A mark-sense reader was used at Scripps Clinic to scan for completeness and to conduct some broad-based logic checks. Any forms containing missing, incomplete, or contradictory examination results were returned to the examining physician for completion before the participants left the site. Any questionable results or "hard-to-diagnose" conditions (such as heart sounds or peripheral pulses) were verified by the diagnostician at the outbriefing. In addition, any differences in interpretation among examiners were identified, and adjustments in recording protocols and programmed data extraction were made as necessary. All examination forms were signed by the examining physician, and the examiner identification number was coded in the database.

6.4.4 Data Completeness Checks

Customized programming of the OMR allowed for the identification of those forms (and their corresponding data records) with missing responses, as well as those with multiple responses to questions that required a single response. The OMR scanner was programmed to reject forms that failed

completeness and multiple response checks and to generate a control code for each rejected form. The control code identified the location of all verification checks failed for a given form.

When a data collection form was rejected, the reason for the rejection was determined. The exact data element was then corrected by comparing the rejected form to the values recorded in the data record created by the scanner. Some of the rejected forms did not contain actual data errors, but rather anomalies created in using mark-sense forms for data collection. For example, the scanner incorrectly counted incompletely erased responses and missed responses marked with too little carbon or graphite. In addition, examiners tended to mark responses clearly for abnormal findings and to mark responses lightly or to bypass responses for expected or desired findings. Failure of the form to provide the correct number of expected responses always resulted in rejection. These errors were resolved, as were the anticipated, more traditional errors.

Out-of-range results and data omissions were monitored to detect trends, possible bias situations, and other data-quality problems. This information was reviewed and relayed to examiners and internal auditors to assist in preventing or correcting chronic, but avoidable, problems. Refresher training was provided to examining physicians to avoid data omissions. Physicians were consulted to correct clinical data, and laboratory out-of-range results were reviewed for logical validity by an independent clinician.

6.4.5 Data Validation

Data files were examined in a series of verification and validation procedures developed to check the results within each participant's record for logical consistency and abnormal findings. Any records noted to have ambiguous findings, incongruent observations, extreme results, errors, or omissions were listed and submitted for review to a physician. Data items that could not be definitively validated or recovered through consultation with the original examiner were assigned codes noting missing or invalid data values. Some reasons for unavailable data included the following:

- Participant refusal
- Unscorable psychological tests
- Test not ordered (e.g., immunology tests, which were only ordered for a subset of the participants)
- Exemption from testing (e.g., exemption from postprandial glucose testing because of diabetes).

These unrecoverable data were excluded from subsequent analysis. The number of values not available for analyses is presented in each clinical chapter by variable.

In the validation process, transcription errors were found between the two dermatology data collection forms. Although these data were not to be analyzed for this report, all forms were manually checked and corrections were made by the dermatologist.

In validating the genitourinary data, SAIC found 14 participant records with inconsistent information. In all cases either the right testis, or both the left and right testes, were not indicated as normal or abnormal. Scripps Clinic physicians reviewed the records and concluded that the intention had been to code the testes normal. These results were recoded to reflect that finding. All changes were noted on the data collection forms.

All laboratory outliers were reviewed and adjudicated by an auditing physician. Each outlier was adjudicated using the following four codes:

1. Clinically explained or plausible (participant has single outlier)
2. Clinically explained or plausible (participant has multiple outliers)
3. Abnormal outlier not clinically explained but plausible
4. Abnormal outlier not clinically explained and not plausible.

These clinical judgments were included in the processing files. In the 1997 follow-up study, no laboratory outliers were coded as "4."

6.5 MEDICAL RECORDS CODING QC

SAIC forwarded completed physical examination records and questionnaire data to the Air Force at Brooks Air Force Base, Texas, for diagnostic coding and verification of all subjectively reported conditions. The Air Force used the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) for morbidity coding; the Systematized Nomenclature of Medicine for anatomic site coding; and the American Hospital Formulary Service for medication coding. Two medical records technicians independently processed each questionnaire and physical examination. Both codings were then subjected to a 100-percent QA review, during which every posted code was checked against medical records. A third medical records technician adjudicated any discrepancies.

6.6 STATISTICAL ANALYSIS QC

Specific QC measures were developed for the statistical analysis efforts. The tasks requiring QC included construction of databases for the analysis of each clinical chapter, the statistical analysis itself, and the preparation of the clinical chapters.

Each specialized statistical database was constructed by defining and locating every variable within the many subparts of the composite follow-up database. Although the data had been subjected to QA procedures during collection, statistical checks for outliers and other improbable values were conducted. Anomalies identified by the statisticians were discussed with those responsible for the data collection (i.e., NORC, Scripps Clinic, or the Air Force).

QA largely depended on regular communication and general agreement among statisticians. Several meetings and consultations between the Air Force team and SAIC statisticians were held in conjunction with the development of the data analysis plan. In addition, many telephone conversations took place during the course of the physical examination. During the analysis, there were frequent telephone conversations, and any problems identified in the statistical analysis were resolved by team discussion. Specialized SAS® programs were developed by the task manager for each type of analysis (exposure, longitudinal, dependent variable-covariate associations) and form of the dependent variable (continuous, dichotomous, polytomous). The software was checked by comparing results from analyses on the same variable by different programs. These programs were adapted for use in all clinical areas by changing the data source, dependent variable, covariates, and exclusions, so that a consistent statistical methodology could be applied to all clinical areas. Modifications to the programs were made only as necessary (e.g., a sparse number of abnormalities that necessitated the exclusion of a particular covariate). Each analysis and the summary statistics reported for the analysis were replicated independently by a separate statistician. The analyses were conducted in accordance with the data analysis plan, which was reviewed

extensively by SAIC and the Air Force. Throughout the study, the Air Force and SAIC maintained duplicate databases. Upon completion of the analyses, SAIC delivered all analysis software and SAS® data sets for each clinical area to the Air Force for final review and archiving.

All tables and statistical results were checked against the computer output from which they were derived, and all statistical statements in the texts were checked for consistency with the results given in the tables. In addition, drafts of each chapter in this report were reviewed by the Air Force and SAIC investigators.

6.7 ADMINISTRATIVE QA

In recognition of the magnitude, complexity, and importance of the AFHS, SAIC created an internal Quality Review Committee (QRC). The QRC was established at the initiation of the 1985 follow-up and continued through the 1987, 1992, and 1997 follow-up studies. Its purpose was to provide general oversight to the AFHS program and advice on the appropriateness of program management and QC actions. The QRC comprised SAIC senior corporate personnel and consultants. These independent reviewers remained separate from the project management staff. The QRC met periodically to review study progress and any issues that either had an impact on study quality or were perceived as a potential problem. Members of the QRC also conducted first-hand evaluations of ongoing program operations.

REFERENCES

1. Westgard, J. O., and P. L. Barry. 1986. Cost-effective quality control: managing the quality and productivity of analytical processes. Washington, DC: AACC Press.

2. Westgard, J. O., J. J. Seehafer, and P. L. Barry. 1994. Allowable imprecision for laboratory tests based on clinical and analytical test outcome criteria. *Clinical Chemistry* 40:1909-14.

Table of Contents

List of Tables

7 STATISTICAL METHODS

7.1 INTRODUCTION

This chapter summarizes the statistical methods used in the analysis of Air Force Health Study (AFHS) 1997 follow-up examination data to investigate relations between the health status of the 2,121 participants attending this examination and their corresponding group (Ranch Hand or Comparison) or serum dioxin estimates and measurements. Group contrast models were similar to analyses performed for the 1982 baseline and 1985, 1987, and 1992 follow-up examinations (1, 2, 3, 4). Models relating health to dioxin estimates and measurements were based on analyses performed for the Serum Dioxin Analysis Report for the 1987 Follow-up and 1992 follow-up examinations (4, 5).

The statistical methods used in this report encompassed four different forms of hypotheses or models applied to 266 study endpoints. Each of these models specified the study cohort or subset of participants included in the respective analyses together with the dioxin exposure or proxy estimates used in the analysis. The first model (Model 1) specified contrasts between Ranch Hands and Comparisons using group as a proxy for exposure, and it did not incorporate serum dioxin measurements. The remaining three models (Models 2, 3, and 4) all incorporated serum dioxin measurements. A summary description of each of the four models is provided in section 7.2, "Models and Assumptions."

Each model and exposure estimate combination was implemented for study variables and type of analysis (unadjusted, adjusted, or longitudinal). The specific statistical procedures (e.g., analysis of variance or logistic regression) that were used are presented in section 7.3, "Factors Determining Statistical Analysis Method." The relation between the factors and statistical procedures is presented in section 7.4, "Analysis Methodologies." That presentation is followed by a discussion of "Interpretive Considerations" (section 7.5), and a description of the contents of tables used to report statistical analysis results throughout the report is given in the "Explanation of Tables" (section 7.6).

7.2 MODELS AND ASSUMPTIONS

The statistical analysis was based primarily on four models, each using a different estimate of exposure. The first model used group and military occupation (officer, enlisted flyer, and enlisted groundcrew) to assess health effects and dose-response relations related to herbicide exposure. Serum dioxin measurements were not used in this model. The other three models accounted for dioxin effects either through estimated initial dioxin levels for Ranch Hands or using current or recent serum dioxin levels for Ranch Hands and Comparisons to assess health endpoints (e.g., cholesterol, diabetes) and dose-response relations related to exposure. These analyses were accomplished with and without adjustment for covariates.

Throughout this report, dioxin levels are used as measures of both exposure to dioxin itself and exposure to dioxin-contaminated herbicides, including Herbicide Orange. Direct contrasts of Ranch Hand and Comparison veterans (Model 1) address the hypothesis of health effects attributable to any herbicide exposure experienced by Ranch Hand veterans during Operation Ranch Hand. Models involving dioxin measurements address the hypothesis that health effects change with the amount of exposure. Dioxin measurements are used as a measure of exposure to dioxin-contaminated herbicides because it is expected that as exposure to such herbicides increased, dioxin levels should increase. Therefore, the dioxin measurement serves as direct biomarker of exposure to dioxin-contaminated herbicides. No other

direct measure or estimate of herbicide exposure is available with which to address hypothetical dose-response relations with health. Some indirect measures, such as self-report of skin contact among enlisted groundcrew, or simply being a Ranch Hand enlisted groundcrew member, are valuable alternatives because dioxin measures suggest that enlisted groundcrew experienced the heaviest exposures. Reported skin exposure is not addressed in this report, but enlisted groundcrew status is addressed in Model 1. The use of dioxin as a measure of exposure to dioxin-contaminated herbicides is consistent with the goal of the study, which is to determine whether health effects exist and can be attributed to occupational exposure to Herbicide Orange (6).

7.2.1 Model 1: Group and Occupation as Estimates of Exposure

This section describes the model that used the exposure group (Ranch Hand, Comparison) to assess the relation between health status and dioxin exposure. Statistical analyses based on this model were termed "Model 1" in the assessment of the clinical areas. Analyses of this type are straightforward, easy to interpret, and well established in epidemiological studies. In this model, exposure was defined as "yes" for Ranch Hands and "no" for Comparisons without regard to the magnitude of the exposure. As an attempt to quantify exposure, three contrasts of Ranch Hands and Comparisons were performed along with the overall Ranch Hand versus Comparison contrast. These three contrasts compared Ranch Hands and Comparisons within each occupational category (officers, enlisted flyers, and enlisted groundcrew). As described in the analyses performed for the Serum Dioxin Analysis Report for the 1987 Followup (5), the average levels of exposure to dioxin were highest for enlisted groundcrew, followed by enlisted flyers, then officers.

Table 7-1 provides a description of Model 1 and gives the assumptions, advantages, and disadvantages for a continuously distributed health endpoint, y. The model presented in Table 7-1 is unadjusted for any covariates—adjusted models are a straightforward extension.

Table 7-1. Model 1: Assessing Health versus Group Status in Ranch Hands and Comparisons: Assumptions, Advantages, and Disadvantages

Model 1:	**$y = \mu + G_i + e$ (All Ranch Hands and Comparisons)** **$y = \mu + G_i + O_j + (GO)_{ij} + e$ (Ranch Hands and Comparisons by occupation)**
where	
y =	health variable in group i and occupation j
G_i =	effect due to group status (i = 1,2 – Comparisons, Ranch Hands)
O_j =	effect due to occupation (j = 1,2,3 – Officers, Enlisted Flyers, Enlisted Groundcrew)
$(GO)_{ij}$ =	interaction between group status and occupation (i = 1,2; j = 1,2,3); used to examine Ranch Hand and Comparison differences for each occupation
e =	zero mean error.
Assumptions:	Comparisons were unexposed and Ranch Hands were exposed. For the purposes of investigating dose-response effects, enlisted groundcrew were more heavily exposed than enlisted flyers, and enlisted flyers were more heavily exposed than officers. The error variance does not change with group status or occupation.
Advantages:	Easily interpretable.
Disadvantages:	Results are biased toward the null hypothesis of no dioxin effect if unexposed Ranch Hands are misclassified (i.e., remain in the analysis as exposed Ranch Hands). It is not possible to fully distinguish unexposed Ranch Hands from exposed Ranch Hands.

7.2.2 Models 2 through 4: Serum Dioxin as an Estimate of Exposure

Current dioxin levels in 1987 were determined by the Centers for Disease Control and Prevention from serum samples taken from approximately 2,000 Ranch Hands and Comparisons. Additional serum samples were taken from selected Ranch Hands and Comparisons at the 1992 and 1997 follow-up examinations to provide insight on dioxin levels and the elimination of dioxin from the body, and to provide measurements for new subjects and those who were not previously measured. A discussion of the details of dioxin measurement is found in Chapter 2, Dioxin Assay.

Investigation of the mechanics of dioxin elimination is currently under study by the Air Force. Based on samples collected in 1982, 1987, 1992, and 1997, issues such as half-life estimation and first-order pharmacokinetic assumptions are being investigated.

7.2.2.1 Prior Knowledge Regarding Dioxin

This section presents analytic strategies based on assumptions and models conceived after the Ranch Hand half-life study published in 1996 (7). Available data have suggested that the dioxin elimination process is first-order, based on measurements subsequent to the ingestion of dioxin by an individual (8). Data on 213 Ranch Hand veterans with dioxin measured in blood collected in 1982, 1987, and 1992 produced a half-life estimate of 8.7 years (7); this estimate was used in all calculations involving half-life.

The term "elimination" denotes the overall removal of dioxin from the body. Some of the analyses assumed that the amount of dioxin in the body (C) decreases exponentially with time according to the model $C = I \cdot \exp(-rt)$, where I is the initial level, $r = \log(2)/h$ is the elimination rate, h is the half-life, and t is the number of years from the end of service in Southeast Asia (SEA) to the time of the blood measurement for dioxin. If a participant had measurements at more than one point in time, the measurement closest to the time of duty in SEA was used. This exponential elimination law is termed "first-order elimination."

The first-order elimination assumption is equivalent to assuming a one-compartment model for dioxin distribution within the body. While a multicompartment model incorporating body composition and dioxin binding to tissue receptors would provide a detailed description of dioxin concentrations in different compartments, published multicompartment models for dioxin distribution within the body predict first-order elimination of dioxin, overwhelmingly because of fecal elimination (9).

The lipid-weight concentration of dioxin, expressed in parts per trillion (ppt) (10, 11), is a derived quantity calculated from the formula $ppt = ppq \cdot 102.6/W$, where ppt is the lipid-weight concentration, ppq (parts per quadrillion) is the actual whole weight of dioxin in the sample in femtograms, 102.6 corrects for the average density of serum, and W is the total lipid weight of the sample (9).

The relation between the serum lipid-weight concentration of dioxin and lipid-weight concentrations in adipose tissue is a subject of continuing research. The correlation between the serum lipid-weight concentration and adipose tissue lipid-weight concentration of dioxin has been observed by Patterson, et al., to be 0.98 in 50 persons from Missouri (12). Using the same data, Patterson, et al., calculated the partitioning ratio of dioxin between adipose tissue and serum on a lipid-weight basis as 1.09 (95% confidence interval: [0.97,1.21]). On the basis of these data, a one-to-one partitioning ratio of dioxin between lipids in adipose tissue and the lipids in serum could not be excluded. Measurements of dioxin in adipose tissue generally have been accepted as representing the body burden concentration of dioxin. The high correlation between serum dioxin levels and adipose tissue dioxin levels in the Patterson, et al., study suggests that serum dioxin is also a valid measurement of dioxin body burden.

7.2.2.2 Fundamental Limitations of the Serum Dioxin Data

There are two evident limitations to the available data:

- While Ranch Hand data did not appear to violate a first-order elimination assumption, no serially repeated dioxin assay results, taken over many years and with which to evaluate directly the adequacy of the first-order elimination model in humans, were available.
- It was not known whether Ranch Hands with body burdens of dioxin at or below 10 ppt were exposed and their body burdens had decreased to these levels since their time of duty in SEA, or whether they were not exposed at all during their time of duty in SEA.

7.2.2.3 Model 2: Health versus Initial Dioxin in Ranch Hands

The relation between estimated initial dioxin levels and health was assessed in Ranch Hands using the model described in Table 7-2. Statistical analyses based on this model were termed "Model 2" in the assessment of the clinical areas. In this model, an initial dioxin level was estimated for a Ranch Hand from a current or recent lipid-adjusted dioxin measure, the length of time between the time of duty in SEA and the date of the blood measurement of dioxin, and an estimated half-life of 8.7 years. From studies conducted by the Air Force, body fat at the time of the blood measurement of dioxin appeared to be related to the dioxin half-life for a participant (7). Hence, this body fat measure was included in this

model as a covariate. Model 2 differs from Model 1 in that the estimate of exposure in Model 1 (group: Ranch Hand, Comparison) was not dependent upon extrapolation to an earlier date.

Table 7-2 also includes assumptions, advantages, and disadvantages of the model for a continuously distributed health variable, y. The model presented in Table 7-2 is unadjusted for any additional risk factors, but extension to an adjusted model is straightforward.

Table 7-2. Model 2: Assessing Health versus Initial Dioxin in Ranch Hands: Assumptions, Advantages, and Disadvantages

Model 2: $y = b_0 + b_1\log_2(I) + b_2BF + e$

where

y	=	health variable
I	=	extrapolated initial dose, assuming first-order elimination, $I = 4+(C-4) \bullet \exp(\log(2) \bullet t/h)$, where 4 ppt is considered the median background level of lipid-adjusted dioxin; t = length of time between the time of duty in SEA and the date of the blood measurement of dioxin in 1987, 1992, or 1997; C = lipid-adjusted dioxin, determined in 1987, 1992, or 1997; and h = dioxin half-life in Ranch Hands assuming first-order elimination (8.7 years assumed for analysis)
BF	=	body fat at the time of the blood measurement of dioxin, calculated from the formula shown below
e	=	zero mean error.

Body fat was calculated from a metric body mass index (13); the formula is

$$\textit{Body Fat (in percent)} = \frac{\textit{Weight (kg)}}{[\textit{Height (m)}]^2} \bullet 1.264 - 13.305.$$

Assumptions: Ranch Hands received a single dioxin dose in Vietnam and background exposure thereafter.
Ranch Hands experienced first-order dioxin elimination.
The error variance does not change with health status or initial dioxin dose.

Advantages: Easily interpretable.
Most efficient if first-order elimination and half-life are valid and y is linearly related to $\log_2(I)$.
The logarithm (base 2) of initial dioxin presents the dioxin data as a more symmetric distribution than the distribution of initial dioxin in its original units. In addition, the relative risk based on the logarithm (base 2) of initial dioxin is more meaningful than on the original scale (i.e., a doubling of initial dioxin rather than a 1 ppt increase in dioxin).

Disadvantages: Results are biased if first-order elimination or constant half-life assumptions are not valid.

In Table 7-2, the phrase "single dioxin dose" is a simplification of the process by which Ranch Hands accumulated dioxin during their time of duty in SEA. This process, which undoubtedly varied from individual to individual, is unknown; however, the time of duty in SEA for an individual Ranch Hand generally was short (1 to 3 years) relative to the time elapsed since his duty in SEA. Hence, additional knowledge regarding the accumulation of dioxin during an individual Ranch Hand's time of duty in SEA, were it to become available, would not likely change conclusions drawn from any of the statistical analyses.

Analyses were performed on Ranch Hands who had lipid-adjusted dioxin levels greater than 10 ppt at either the 1987, 1992, or 1997 physical examinations. The value 10 ppt corresponds to the approximate 98th percentile of the Comparison lipid-adjusted dioxin distribution. Based on this Comparison dioxin distribution, it was believed that participants with greater than 10 ppt lipid-adjusted dioxin were definitely exposed. It was not known whether Ranch Hands with dioxin burdens at or below 10 ppt were exposed and their body burdens had decreased to these levels since their time of duty in SEA, or whether they were not exposed at all during their time of duty in SEA. Lipid-adjusted dioxin levels less than 10 ppt are subsequently called "background" levels.

7.2.2.4 Model 3: Health versus Dioxin in Ranch Hands and Comparisons

An assessment of the health consequences of dioxin above background levels was carried out with a model that was applied to both Ranch Hand and Comparison data. This model assessed health versus dioxin body burden categorized into four levels, given below:

- Comparisons—Comparisons with up to 10 ppt lipid-adjusted dioxin
- Background—Ranch Hands with up to 10 ppt lipid-adjusted dioxin
- Low—Ranch Hands with more than 10 ppt lipid-adjusted dioxin but at most 94 ppt estimated initial dioxin
- High—Ranch Hands with more than 10 ppt lipid-adjusted dioxin and more than 94 ppt estimated initial dioxin.

Statistical analyses based on this model were termed "Model 3" in the assessment of the clinical areas. The low and high Ranch Hand categories, of approximately equal size, were determined by the median estimated initial dioxin level (94 ppt) of the Ranch Hands with more than 10 ppt lipid-adjusted dioxin (i.e., the sample used in Model 2). In this model, an initial dioxin level was estimated for a Ranch Hand from a current or recent lipid-weight dioxin measure, the length of time between the time of duty in SEA and the date of the blood measurement of dioxin, and an estimated half-life of 8.7 years. From studies conducted by the Air Force, body fat at the time of the blood measurement of dioxin appeared to be related to the dioxin half-life for a participant. This body fat measure was included in this model as a covariate. Using this body fat measure in Model 3 for all Comparisons and Ranch Hands with dioxin measurements allowed body fat to act as a potential risk factor as well as an adjusting variable to explain half-life differences.

For a continuously distributed health variable, y, for example, the mean values of y within the background, low, high, and low plus high categories were contrasted with the mean values of y within the Comparison category. The mean value of y for the low plus high category was calculated as a linear combination of the low dioxin category and the high dioxin category, with weights based on the sample size in each of these categories. Relative frequencies were contrasted for discrete health variables. Table 7-3 shows this model and the assumptions, advantages, and disadvantages for the unadjusted analysis of a continuous variable; extension to an adjusted model is straightforward.

Table 7-3. Model 3: Assessing Health versus Categorized Dioxin in Ranch Hands and Comparisons

Model 3: $y = b_0 + b_1I_1 + b_2I_2 + b_3I_3 + b_4I_4 + b_5BF + e$

where

y	=	health variable
I_1	=	indicator variable for categorized dioxin; $I_1 = 1$ if participant is a Comparison with a background level of dioxin, $I_1 = 0$ if participant is not a Comparison
I_2	=	indicator variable for categorized dioxin; $I_2 = 1$ if participant is in background dioxin category, $I_2 = 0$ if participant is not in background dioxin category
I_3	=	indicator variable for categorized dioxin; $I_3 = 1$ if participant is in low dioxin category, $I_3 = 0$ if participant is not in low dioxin category
I_4	=	indicator variable for categorized dioxin; $I_4 = 1$ if participant is in high dioxin category, $I_4 = 0$ if participant is not in high dioxin category
BF	=	body fat at the time of blood measurement of dioxin, calculated from the formula shown below
e	=	zero mean error.

Body fat was calculated from a metric body mass index (13); the formula is

$$Body\ Fat\ (in\ percent) = \frac{Weight\ (kg)}{[Height\ (m)]^2} \bullet 1.264 - 13.305.$$

Assumptions:	Dioxin body burden has been eliminated with time. The error variance does not change with categorized dioxin body burden.
Advantages:	Initial dioxin is probably a better measure for determining low and high exposure than current or recent lipid-adjusted dioxin measurements. Less dependent on the accuracy of the estimation algorithm for determining initial dioxin than Model 2.
Disadvantages:	Makes no use of prior belief that some Ranch Hands received an unusually large dioxin dose in Vietnam; all Ranch Hands with high dioxin levels are treated similarly. "Background" Ranch Hand category is probably a mixture of exposed and unexposed Ranch Hands. Analysis may be biased toward the null hypothesis of no dioxin effect. "Low" and "high" Ranch Hand categories are based on initial dioxin model, which is based on valid half-life and first-order dioxin elimination. Bias is possible if model is incorrect. Also, a conditional null hypothesis is tested using these categories ("Is there a dioxin effect, given a specified level of exposure?").

7.2.2.5 Model 4: Health versus 1987 Dioxin in Ranch Hands

The relation between 1987 dioxin and health was assessed using the model described in Table 7-4. This measure of dioxin is termed "1987 dioxin" because most Ranch Hands were assayed for dioxin initially at the 1987 follow-up examination. This table also describes the assumptions, advantages, and disadvantages for the unadjusted analysis of a continuously distributed health variable, y.

Ranch Hands with a dioxin measurement may have had their blood collected at the pilot study in April 1987, at the 1987 physical examination, at the 1992 physical examination, or at the 1997 physical examination. If an individual had measurements at more than one of these points in time, the measurement closest to the time of duty in SEA was used. If only a 1992 serum dioxin measurement was available, the level was extrapolated to the date of the 1987 physical examination. The model

$$C_{1987} = 4+(C_{1992}-4) \bullet \exp(rt)$$

was used for extrapolation of lipid-adjusted dioxin to 1987 levels (C_{1987}), where C_{1992} is the lipid-adjusted dioxin level in 1992, 4 ppt is considered the median background level for lipid-adjusted dioxin, $r = \log(2)/h$ is the elimination rate, h is the half-life (8.7 years), and t is the length of time between the physical examination in 1987 and the physical examination in 1992. This model was used only if the lipid-adjusted dioxin level in 1992 was greater than 10 ppt; otherwise, the 1992 measurement was used. A similar strategy was used for participants who had only a 1997 serum dioxin measurement. The estimate of exposure in Model 4 (1987 dioxin) was based on extrapolation to 1987 for only 39 out of the 863 Ranch Hands. Most measurements were based on 1987 dioxin measurements and extrapolation was not needed. Consequently, body fat at the time of the blood measurement of dioxin was not used in Model 4, which was different from the strategy used for Models 2 and 3.

Table 7-4. Model 4: Assessing Health versus 1987 Dioxin in Ranch Hands: Assumptions, Advantages, and Disadvantages

Model 4: $\mathbf{y = b_0 + b_1\log_2(ppt+1) + e}$

where

y	=	health variable
ppt	=	lipid-adjusted dioxin = ppq•102.6/W, where ppq = whole weight of dioxin in the sample in femtograms (102.6 corrects for the average density of serum) and W = total lipid weight of the sample
e	=	zero mean error.

Assumptions:	Ranch Hands received a single dioxin dose in Vietnam and background exposure thereafter. The error variance does not change with health status or 1987 dioxin.
Advantages:	Using 1987 dioxin has less inherent variation than initial dioxin, which is extrapolated by a first-order elimination model across a 20- to 30-year time period. The logarithm (base 2) of (1987 dioxin + 1) presents the dioxin data as a more symmetric distribution than the distribution of 1987 dioxin in its original units. In addition, the relative risk based on the logarithm (base 2) of (1987 dioxin + 1) is more meaningful than on the original scale (i.e., a doubling of 1987 dioxin + 1, rather than a 1 ppt increase in dioxin).
Disadvantages:	1987 dioxin may not be a good surrogate for exposure if elimination rate differs among individuals. Individuals with measurements in 1992 only or 1997 only are extrapolated to 1987, and variation is increased with estimation using a first-order elimination model.

The relation between current health and dioxin was assessed using a model, termed "Model 4," with lipid-adjusted 1987 dioxin as the estimate of exposure. Model 4 used the logarithm (base 2) of lipid-adjusted 1987 dioxin and is described in Table 7-4.

7.3 FACTORS DETERMINING THE STATISTICAL ANALYSIS METHOD

For a specified questionnaire-based or clinical measurement determined from the physical or laboratory examination, the selection of an analytical method depended on each of the following:

- Dependent Variable Form: Continuous or discrete
- Exposure Estimate and Analysis Cohort:
  - Model 1: Group—All Ranch Hands and Comparisons
  - Model 2: Initial dioxin—Ranch Hands having a dioxin body burden of greater than 10 ppt of lipid-adjusted dioxin, based on 1987 dioxin levels as defined in Section 7.2.2.5
  - Model 3: Categorized dioxin—Comparisons with a dioxin body burden of 10 ppt lipid-weight dioxin or less, based on 1987 dioxin levels, and all Ranch Hands with a dioxin measurement
  - Model 4: 1987 dioxin—All Ranch Hands with a dioxin measurement
- Analysis Type: Unadjusted, adjusted, or longitudinal.

Table 7-5 specifies 22 separate analysis situations based on dependent variable form, exposure estimate, analysis cohort, and analysis type. For each of the 22 situations, the statistical method is specified. For example, linear regression models were used for adjusted analyses of initial dioxin for continuous dependent variables.

Table 7-5. Summary of Statistical Analysis Situations by Dependent Variable Form, Exposure Estimate, Analysis Cohort, and Analysis Type

Exposure Estimate	Analysis Cohort	Analysis Type	Statistical Methods	Independent Variables
		Continuous		
Model 1: Group (Ranch Hands vs. Comparisons)	All RH & C	Unadjusted	Analysis of Variance	Group
		Adjusted	Analysis of Covariance	Group; Covariates
		Longitudinal[a]	Analysis of Covariance	Group; Age at the 1997 Follow-up Examination; 1982 Measurement
Model 2: Log_2(Initial)	RH >10 ppt lipid-adjusted 1987 dioxin	Unadjusted	Linear Regression	Log_2(Initial); Body Fat at the Time of the Blood Measurement of Dioxin
		Adjusted	Linear Regression	Log_2(Initial); Body Fat at the Time of the Blood Measurement of Dioxin; Covariates

Table 7-5. Summary of Statistical Analysis Situations by Dependent Variable Form, Exposure Estimate, Analysis Cohort, and Analysis Type (Continued)

Exposure Estimate	Analysis Cohort	Analysis Type	Statistical Methods	Independent Variables
		Longitudinal[a]	Linear Regression	Log_2(Initial); Body Fat at the Time of the Blood Measurement of Dioxin; Age at the 1997 Follow-up Examination; 1982 Measurement
Model 3: Categorized Dioxin	All RH with a dioxin measurement, C ≤10 ppt lipid-adjusted 1987 dioxin	Unadjusted	Analysis of Covariance	DXCAT; Body Fat at the Time of the Blood Measurement of Dioxin
		Adjusted	Analysis of Covariance	DXCAT; Body Fat at the Time of the Blood Measurement of Dioxin; Covariates
		Longitudinal[a]	Analysis of Covariance	DXCAT; Body Fat at the Time of the Blood Measurement of Dioxin; Age at the 1997 Follow-up Examination; 1982 Measurement
Model 4: Log_2 (1987 Dioxin +1)	All RH with a dioxin measurement	Unadjusted	Linear Regression	Log_2(1987 Dioxin + 1)
		Adjusted	Linear Regression	Log_2(1987 Dioxin + 1); Covariates
		<u>Discrete</u>		
Model 1: Group (Ranch Hands vs. Comparisons)	All RH & C	Unadjusted	Chi-Square Contingency Table, Logistic Regression	Group
		Adjusted	Logistic Regression	Group; Covariates
		Longitudinal[b]	Logistic Regression	Group; Age at the 1997 Follow-up Examination
Model 2: Log_2(Initial)	RH >10 ppt lipid-adjusted 1987 dioxin	Unadjusted	Logistic Regression	Log_2(Initial); Body Fat at the Time of the Blood Measurement of Dioxin
		Adjusted	Logistic Regression	Log_2(Initial); Body Fat at the Time of the Blood Measurement of Dioxin; Covariates
		Longitudinal[b]	Logistic Regression	Log_2(Initial); Body Fat at the Time of the Blood Measurement of Dioxin; Age at the 1997 Follow-up Examination
Model 3: Categorized Dioxin	All RH with a dioxin measurement, C ≤10 ppt lipid-adjusted 1987 dioxin	Unadjusted	Chi-Square Contingency Table; Logistic Regression	DXCAT; Body Fat at the Time of the Blood Measurement of Dioxin
		Adjusted	Logistic Regression	DXCAT; Body Fat at the Time of the Blood Measurement of Dioxin; Covariates

Table 7-5. Summary of Statistical Analysis Situations by Dependent Variable Form, Exposure Estimate, Analysis Cohort, and Analysis Type (Continued)

Exposure Estimate	Analysis Cohort	Analysis Type	Statistical Methods	Independent Variables
		Longitudinal[b]	Logistic Regression	DXCAT; Body Fat at the Time of the Blood Measurement of Dioxin; Age at the 1997 Follow-up Examination
Model 4: Log_2 (1987 Dioxin + 1)	All RH with a dioxin measurement	Unadjusted	Logistic Regression	Log_2 (1987 Dioxin + 1)
		Adjusted	Logistic Regression	Log_2 (1987 Dioxin + 1); Covariates

[a] Dependent variable usually paired difference score of (1997 to 1982) dependent variable values. For some clinical areas, paired difference scores were (1997 to 1985) differences.
[b] Analysis performed subject to the constraint that participant was normal at the 1982 baseline (or 1985) examination.

Note: Log_2 (Initial) = Logarithm (base 2) of estimated initial dioxin level.
Log_2 (1987 Dioxin + 1) = Logarithm (base 2) of (1987 dioxin level + 1).
DXCAT = Categorized dioxin (incorporating group membership—three categories for Ranch Hands, one category for Comparisons).
RH = Ranch Hand.
C = Comparison.

7.4 ANALYSIS METHODOLOGIES

7.4.1 Methods for Analyzing Continuous and Discrete Variables

For analyses of continuous dependent variables, the general linear models approach was used for applying such techniques as simple and multiple linear regression, analysis of variance, analysis of covariance, repeated measures analysis, and survival time analysis. This approach permitted model fitting of the dependent variable as a function of group or dioxin and specified covariates. Continuous dependent variables were examined to ensure that assumptions underlying appropriate statistical methods were met. Transformations (e.g., square root, logarithmic) were used to enhance normality for specific continuous health variables. A further discussion of general linear models, as well as other methods used for the statistical analyses in this report, is found in Table 7-6.

For these continuous analyses, the SAS®[1] general linear models analysis (PROC GLM) (14) was used. After a model was fitted, tests of significance for a group or dioxin effect were developed. Associations with a p-value less than or equal to 0.05 were described as significant, and associations with a p-value greater than 0.05 but less than or equal to 0.10 were described as marginally significant.

The SAS® procedures LIFEREG and LIFETEST (14) were used for the time to diabetes onset variable in the endocrine clinical assessment. Statistical methods used to analyze measures of this type implemented

[1] SAS and all other SAS Institute, Inc., product and service names are registered trademarks or trademarks of SAS Institute, Inc., in the USA and other countries.

a technique known as "survival time" analysis. A further discussion of survival time analysis is found in Table 7-6.

For dichotomous discrete dependent variables, logistic regression was performed using SAS® PROC GENMOD (15). For dependent variables with more than two categories, polytomous logistic regression was performed using SAS® PROC CATMOD (14). Parameter estimation and model selection for polytomous logistic regression and ordinary logistic regression are similar. Both forms of regression use the maximum likelihood principle to obtain parameter estimates. For a model with k parameters for two equations, 2k parameters are estimated, k for each logit function. If ordinary logistic regression is applied twice (for example, once for abnormal low versus normal and then for abnormal high versus normal), 2k parameters are estimated; however, ordinary logistic regression maximizes two likelihood equations, each with k parameters, while polytomous logistic regression estimates all 2k parameters simultaneously with one likelihood equation. Polytomous logistic regression also can be used for dependent variables that have more than three levels and require more than two contrasts with a normal category. A further discussion of logistic regression and polytomous logistic regression is found in Table 7-6.

A chi-square statistic, adjusted for the continuity of the chi-square distribution, was used when a test of the relative frequency of abnormal measurements between Ranch Hands and Comparisons was performed, and the relative frequency of either the Ranch Hand or the Comparison group was zero. This test statistic yields p-values approximately equal to Fisher's exact test (16) for a two-sided alternative hypothesis.

Table 7-6. Summary of Statistical Procedures

Chi-Square Contingency Table Test

The chi-square test of independence (17) is calculated for a contingency table by the following formula:

$$\chi^2 = \sum \frac{(f_O - f_E)^2}{f_E}$$

where the sum is taken over all cells of the contingency table and

f_O = observed frequency in a cell

f_E = expected frequency under the hypothesis of independence.

Large values indicate deviations from the null hypothesis and are tested for significance by comparing the calculated χ^2 to the tables of the chi-square distribution.

For 2x2 tables, the chi-square statistic above can be adjusted for the continuity of the χ^2 distribution. This test statistic yields p-values approximately equal to Fisher's exact test (16) for a two-sided alternative and is as follows:

$$\chi^2 = \sum \frac{\max(0, (|f_O - f_E| - \frac{1}{2}))^2}{f_E}.$$

Correlation Coefficient (Pearson's Product-Moment)

The population correlation coefficient ρ (18) measures the strength of the linear relation between two random variables X and Y. A commonly used sample-based estimate of this correlation coefficient is

$$\rho = \frac{\sum (x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\left[\sum (x_i - \bar{x})^2 \sum (y_i - \bar{y})^2\right]}}$$

where the sum is taken over all (x, y) pairs in the sample. A student's t-test based on this estimator is used to test for a significant correlation between the two random variables of interest. For the sample size of approximately 2,121 in this study, a sample correlation coefficient of 0.04254 is sufficient to attain a statistically significant correlation at a 5-percent level for a two-sided hypothesis test, assuming normality of X and Y.

Survival Time Analysis

The survival time model (19) permits a dependent variable with censored observations to be modeled in a general linear models framework. For example, if the time to diabetes onset is defined as an event, the time for participants for which this event has not occurred is right-censored. The survival time model is

$$y = X\beta + \sigma\varepsilon$$

where

y	=	vector of responses (e.g., time to diabetes onset), usually the logarithm of the survival times
X	=	matrix of covariates, or risk factors (e.g., group status and age)
ß	=	vector of unknown regression parameters
σ	=	unknown scale parameter
ε	=	vector of errors assumed to have a known distribution.

For a model with a dependent variable containing right-censored data, the log likelihood function is a combination of a probability density function for noncensored values and a survival distribution function for right-censored values. The model parameters can be estimated by maximum likelihood in SAS® PROC LIFEREG, using a Newton-Raphson algorithm, where the distribution of the random error term can be specified. The distributional assumptions regarding the error term can be tested by examining plots of the Kaplan-Meier survival functions using SAS® PROC LIFETEST.

PROC LIFEREG provides estimates, standard errors, and p-values associated with a chi-square test on each parameter (i.e., risk factor) in the model. These are used to test the significance of the group or dioxin term in the unadjusted and adjusted models. In this procedure, percentile estimates also can be produced for each group or each dioxin category in the unadjusted model. The percentile estimates are used to determine parameter estimates from the Weibull distribution. The Weibull distribution parameter estimates are then used in an iterative nonlinear estimation procedure (SAS® PROC NLIN [14]) to produce estimated means from a censored Weibull distribution. The loss function that is minimized in the estimation procedure is

$$Loss = -\log[x \bullet (\frac{\beta}{\theta^\beta} \bullet y^{\beta-1} \bullet e^{-(\frac{y}{\theta})^\beta}) + (1-x) \bullet (1 - e^{-(\frac{y}{\theta})^\beta})]$$

where x = 1 if diabetic
x = 0 if not diabetic
and y = time to onset of diabetes.

Table 7-6. Summary of Statistical Procedures (Continued)

General Linear Models Analysis

The form of the general linear model (18) for two independent variables is

$$Y = \alpha + \beta_1 X_1 + \beta_2 X_2 + \varepsilon$$

where

Y	=	dependent variable (continuous)
α	=	level of Y at $X_1 = 0$ and $X_2 = 0$ (i.e., the intercept)
X_1, X_2	=	measured value of the first and second independent variables, respectively, which may be continuous or discrete (e.g., group status and age)
β_1, β_2	=	coefficient indicating linear association between Y and X_1, Y and X_2, respectively; each coefficient reflects the effect on the model of the corresponding independent variable adjusted for the effect of the other independent variable
ε	=	error term.

This model assumes that the error terms are independent and normally distributed with a mean of 0 and a constant variance. Extension to more than two independent variables is immediate. Simple linear regression, multiple linear regression, analysis of variance, analysis of covariance, and repeated measures analysis of variance are all examples of general linear models analysis.

Logistic Regression Analysis

The logistic regression model (20) enables a dichotomous dependent variable to be modeled in a regression framework with continuous and discrete independent variables. For two risk factors, such as dioxin and age, the logistic regression model is

$$\text{logit } P = \alpha + \beta_1 X_1 + \beta_2 X_2 + \varepsilon$$

where

P	=	probability of disease for an individual with risk factors X_1 and X_2
logit P	=	ln (P/(1-P)) (i.e., the log odds for disease)
X_1	=	first risk factor (e.g., dioxin)
X_2	=	second risk factor (e.g., age).

The parameters are interpreted as follows:

α	=	log odds for the disease when $X_1 = 0$ and $X_2 = 0$
β_1	=	coefficient indicating the dioxin effect adjusted for age
β_2	=	coefficient indicating the age effect adjusted for dioxin
ε	=	error term.

For a dichotomous measure, the term $\exp(\beta_1)$ equals the adjusted odds ratio of abnormal versus normal for Ranch Hands ($X_1 = 1$) compared to Comparisons ($X_1 = 0$). If the probability of being abnormal is small compared to being normal for both the Ranch Hand and Comparison groups, the odds ratio is approximately equal to the relative risk of being abnormal between the two groups. If X_1 is a continuous covariate, $\exp(\beta_1)$ represents the adjusted odds ratio of outcome 1 versus outcome 0 for a unit increase in X_1. If the risk factor is expressed in logarithmic (base 2) form, $\exp(\beta_1)$ reflects the adjusted odds ratio for a twofold increase in the risk factor. Throughout this report and previous reports, the adjusted odds ratio was referred to as an adjusted relative risk. Correspondingly, in the absence of covariates (i.e., unadjusted analysis), the unadjusted odds ratio was referred to as an estimated relative risk.

This technique also was used for longitudinal analyses of dichotomous dependent variables to examine changes in health status between 1982 (or 1985) and 1997 in relation to the dioxin measures.

Table 7-6. Summary of Statistical Procedures (Continued)

Polytomous Logistic Regression Analysis

Polytomous logistic regression (20, 21) allows a categorical dependent variable with more than two outcomes to be modeled in a regression environment with continuous and discrete independent variables. For polytomous logistic regression, the model equation depends on the scale of the dependent variable. This discussion focuses on nominal scaled dependent variables.

Suppose Y is a nominal scaled dependent variable with three outcomes labeled 0, 1, or 2 (normal, low, or high). Polytomous logistic regression models two logit functions, one for Y = 1 versus Y = 0 and the other for Y = 2 versus Y = 0. The zero outcome for Y is called the reference category. To model Y with two covariates such as group status and age, the polytomous regression model would be

$$\text{logit } P_1 = \alpha_1 + \beta_{1(1)}X_1 + \beta_{1(2)}X_2 + \varepsilon_1$$

$$\text{logit } P_2 = \alpha_2 + \beta_{2(1)}X_1 + \beta_{2(2)}X_2 + \varepsilon_2$$

where

P_i	=	probability that Y = i (outcome i) with covariates X_1 and X_2, i = 0, 1, 2
logit P_i	=	ln (P_i/P_0) (i.e., the log odds of outcome i versus outcome 0, i = 1, 2)
X_1	=	first effect (e.g., group status)
X_2	=	second effect (e.g., age).

The parameters are interpreted as follows:

α_i	=	log odds of outcome i versus outcome 0 when $X_1 = 0$ and $X_2 = 0$, i = 1, 2
$\beta_{i(1)}$	=	coefficient indicating the group status effect on the logit P_i, adjusted for age; i = 1, 2
$\beta_{i(2)}$	=	coefficient indicating the age effect on the logit P_i, adjusted for group status; i = 1, 2
ε_i	=	error term for logit P_i, i = 1, 2.

This model assumes independent multinomial sampling.

Because the interpretation of each logistic modeling function is similar, consider the logit P_1 and suppose X_1 is a binary covariate ($X_1 = 1$ for Ranch Hands or $X_1 = 0$ for Comparisons). The term $\exp(\beta_{1(1)})$ equals the adjusted odds ratio of low versus normal for Ranch Hands ($X_1 = 1$) compared to Comparisons ($X_1 = 0$). If the probability of being low is small compared to being normal for both the Ranch Hand and Comparison groups, the odds ratio of low versus normal is approximately equal to the relative risk of being low between the two groups. If X_1 is a continuous covariate, $\exp(\beta_{1(1)})$ represents the adjusted odds ratio of outcome 1 versus outcome 0 for a unit increase in X_1.

The abnormal and normal categorizations for many of the discrete analyses were defined by categorizing laboratory and physical examination measures according to laboratory and clinic reference values. Cutpoints for the dependent variables erythrocyte sedimentation rate, cholesterol, and total testosterone were age-dependent. Consequently, normal and abnormal levels were constructed according to a participant's laboratory value and age at the physical examination.

7.4.2 Modeling Strategy

In general, based on one of the adjusted analysis models described in Table 7-5, a model for dependent variables was based on the exposure effect (group or dioxin) and medically relevant covariates, as identified in Chapters 9 through 18 for each clinical category. As described previously, body fat at the time of the blood measurement of dioxin was included in Models 2 and 3.

The general modeling strategy did not remove any covariates from the model; however, the modeling strategy for the adjusted analysis of dependent variables in certain clinical areas was modified as necessary because of the large number of covariates or sparse number of participants with abnormal measurements. Stepwise elimination of covariates was conducted to allow for proper estimation of model parameters. When this strategy of removing covariates was necessary, the covariates removed from (or retained in) a model for a given health endpoint and model were specified in footnotes to the tables.

7.4.3 Longitudinal Analysis

Selected longitudinal analyses were performed to investigate changes in health status between 1982 and 1997 for Models 1, 2, and 3 as a function of dioxin exposure. Model 4 was not examined in longitudinal analyses because lipid-adjusted dioxin, the estimate of exposure in this model, changes over time and was not available for all participants in 1982 or 1997. All three models were adjusted for age at the time of the 1997 follow-up physical examination. Age was a well-known risk factor for nearly all clinical areas, and although Ranch Hands and Comparisons were matched on age, the estimates of dioxin exposure in Models 2 and 3 were not.

In the longitudinal analysis of discrete variables, only those participants whose health was classified as normal in 1982 were included in the analysis of the participants' health at the 1997 follow-up examination. Participants classified as "abnormal" in 1982 were excluded because the focus of the analysis was to investigate the temporal effects of dioxin exposure between 1982 and 1997. Participants classified as "abnormal" in 1982 were already abnormal before this period; consequently, only participants classified as "normal" at the 1982 examination were considered to be at risk when the effects of dioxin over time were explored. The rate of abnormalities under this restriction approximated the cumulative incidence rate between 1982 and 1997 (22).

The dependent variable in this type of analysis was the health of participants at the 1997 examination whose health was normal in 1982. The independent variables were the appropriate exposure estimate and age at the time of the 1997 follow-up physical examination. The analyses of Models 2 and 3 also were adjusted for body fat at the time of the blood measurement of dioxin. Tabular displays of the longitudinal analysis results of discrete dependent variables include summary statistics for 1982 and 1997, as well as 1985, 1987, and 1992 summaries, if available. The results of the statistical analysis restricted to those participants who were normal in 1982 also were provided.

In the longitudinal analysis of continuous variables, a general linear model approach, as explained in Table 7-6, was used. The dependent variable was the difference between the 1997 measurement and the 1982 measurement. This difference, measuring the change in the endpoint over this period of time, was modeled as a function of the estimate of exposure (group or dioxin), the participant's age at the time of the 1997 follow-up physical examination, and the 1982 measurement of the continuous dependent variable. The analyses of Models 2 and 3 also were adjusted for body fat at the time of the blood measurement of dioxin. The reasons for using the health endpoint measurement in 1982 for longitudinal analysis of continuous variables were as follows:

- A linear relation between measurements of the dependent variable in 1982 and 1997 because of a difference in measuring devices was accounted for by using the 1982 measurement as an independent variable.
- The difference between two measurements taken over a period of time was generally correlated with the first measurement (23).
- The relation between the difference of the 1997 and 1982 measurements and the estimate of exposure may be confounded with the 1982 measurement, especially if the endpoint and the estimate of exposure were related.

Tabular displays of the results of longitudinal analysis of continuous dependent variables include summary statistics for 1982 and 1997, as well as 1985, 1987, and 1992 summaries, if available. Results of the statistical analysis relating the difference in the 1997 and 1982 measurements to the estimate of exposure also were provided. For some variables, 1985 clinical measurements were substituted for 1982 measurements because the variable was not analyzed at the 1982 examination or was inherently different from the 1997 variable due to differing clinical methods.

7.5 INTERPRETIVE CONSIDERATIONS

Several specific issues to consider when interpreting the results found in this report are discussed in this section. The issues discussed here include adjustments for covariates, multiple testing, trends in the results of endpoints within a clinical area, the proportion of variation explained by the model (R^2), interpretation of discrete and continuous analyses of a health endpoint, and statistical power to detect the effects of dioxin.

7.5.1 Adjustments for Covariates

In contrasts between all Ranch Hands and all Comparisons (Model 1), the matching variables age, race, and occupation were effectively eliminated as confounders. The initial and 1987 dioxin analyses within Ranch Hands (Models 2 and 4) and the categorized dioxin analysis within Ranch Hands and Comparisons (Model 3) did not benefit from the matched design. For example, military occupation was a strong confounder because it is highly correlated with dioxin levels in Ranch Hands and is related to some health variables through socioeconomic differences between officers and enlisted personnel. Education was highly associated with military occupation and certain psychometric results. Consequently, with the exception of a few analyses where the prevalence or history of abnormal results was sparse, all health endpoints were analyzed with and without adjustment for clinically relevant covariates.

7.5.2 Multiple Testing

Numerous dependent variables were considered because of the lack of a predefined medical endpoint. Each dependent variable was analyzed in many different ways to accommodate covariate information and different statistical models. Under the hypothesis of no relation between physical health and dioxin, approximately 5 percent of the many statistical tests (group or dioxin effects) in this report detected an association between group or dioxin and health (p-values ≤ 0.05). Observing significant results because of multiple testing, even when there is no relation between dioxin and health, is known as the multiple-comparisons problem (24) and is common in all large studies with multiple endpoints. It is generally difficult to distinguish between those statistically significant results that arise because of the multiple testing artifact and those that may be due to an actual dioxin effect. In order to weigh and interpret the findings, the strength of the association, consistency, dose-response patterns, and biologic plausibility were considered.

7.5.3 Trends

Assessing consistent and meaningful trends is essential when interpreting any comprehensive study with multiple endpoints, clinical areas, and covariates; however, caution must be used. Increased numbers of abnormalities or mean values with increased dioxin levels across medically related variables within a clinical area might indicate a group or dioxin effect. There may, however, be a moderate-to-strong correlation between these endpoints, where a change in one variable leads directly to a change in the other. Hence, the strength of the trends also was considered when assessing the suspected association.

7.5.4 Interpretation of the Coefficient of Determination

The coefficient of determination (R^2) measures the proportionate reduction of the total variation in a continuously distributed health variable, y, associated with the set of independent variables in a linear regression. A large value of R^2 does not necessarily imply that the fitted model is a useful one. Large values of R^2 would occur, for example, if y is regressed on an independent variable with only a few observed values. On the other hand, small values of R^2 are generally seen in observational studies because little or no control has been applied in the assignment of the values of the "treatment" (dioxin) or the conditions under which the "treatment" has been applied. In this study, the dioxin measurements were taken many years after exposure and are subject to some measurement error. Thus, in most analyses, the values of R^2 were small.

7.5.5 Clinical Interpretation of Discrete versus Continuous Data

Small but significant mean differences in a continuously measured health variable (e.g., alkaline phosphatase) between exposed and unexposed groups when there are no corresponding differences in the percentage of abnormal tests are difficult to interpret in any study. In this study, significant differences in the means between exposed and unexposed groups sometimes are observed without a corresponding difference between the groups in the percentage of participants with an abnormal measurement. Such contrasting situations may be interpreted as spurious outcomes of no clinical consequence, or as a subclinical dioxin effect. Significant trends in the mean with increasing levels of dioxin were interpreted as a dioxin-related effect if a corresponding trend was seen in the proportion above or below the normal range or if the trend was consistent with other findings.

7.5.6 Power

A type I error is making a false conclusion that an association (group or dioxin effect) exists when there is no association. The other possible inference error, a type II error, is the failure to detect an association when one actually exists. The power of a statistical test is 1 minus the probability of a type II error. The power of the test is the probability that the test will reject the hypothesis of no group or dioxin effect when an effect does in fact exist.

The fixed size of the Ranch Hand cohort limits the ability of this study to detect some group or dioxin associations if they exist. This limitation is most obvious for specific types of cancer, such as soft tissue sarcoma (STS) and non-Hodgkin's lymphoma (NHL). These conditions are so uncommon that fewer than two cases are expected in this study, indicating that there is virtually no statistical power to detect low-to-moderate associations between dioxin and cancer. In an attempt to overcome the lack of power to detect group differences for specific types of systemic cancer, for example, all types of systemic cancer were combined into a single variable. It is still possible, however, that an increased risk could exist for a particularly rare type of cancer, allowing that increased risk to be missed in this study.

Table 7-7 and Appendix Tables E-1 through E-3 contain the approximate power at a significance level of 0.05 to detect specified relative risks for a given prevalence rate of a discrete dependent variable. Table 7-7 presents power calculations for Model 1 (group), and Appendix Tables E-1 through E-3 present power calculations for Model 2 (initial dioxin), Model 3 (categorized dioxin—low plus high Ranch Hand versus Comparison contrast), and Model 4 (lipid-adjusted 1987 dioxin). Power calculations were performed using the logarithm (base 2) of dioxin in Models 2 and 4, and consequently, the relative risk is for a twofold increase in dioxin. The power of a test for a discrete variable depends on the significance level, actual relative risk, prevalence of the condition, and the Ranch Hand and Comparison sample sizes (for Models 1 and 3) or the distribution of the dioxin data (for Models 2 and 4).

As an example, using age-adjusted incidence rates for all U.S. males (based on data from the Surveillance Epidemiology and End Results program of the National Cancer Institute), prevalence rates for all cancers, NHL, and STS were estimated as 0.07, 0.002, and 0.001, respectively. Thus, Table 7-7 shows a power less than 0.21 to detect a relative risk of 2.0 for the estimated prevalences of NHL and STS. For a disease with a prevalence of 0.05, the power to detect a relative risk of 1.5 would be 0.54.

Table 7-7. Approximate Power To Detect a Group Effect at a 5-Percent Level of Significance (Discrete Dependent Variable)

Prevalence of Condition	Relative Risk								
	1.10	1.20	1.30	1.40	1.50	1.75	2.00	10.00	20.00
0.005	0.05	0.06	0.07	0.09	0.10	0.15	0.21	0.92	0.97
0.01	0.06	0.07	0.09	0.12	0.16	0.26	0.36	1.00	1.00
0.02	0.06	0.09	0.14	0.19	0.26	0.45	0.62	1.00	1.00
0.03	0.07	0.11	0.18	0.26	0.36	0.60	0.79	1.00	1.00
0.04	0.07	0.13	0.22	0.33	0.45	0.72	0.89	1.00	1.00
0.05	0.08	0.15	0.26	0.40	0.54	0.81	0.94	1.00	1.00
0.10	0.10	0.24	0.44	0.64	0.80	0.97	1.00	1.00	1.00
0.15	0.12	0.32	0.58	0.79	0.92	1.00	1.00	1.00	1.00
0.20	0.14	0.38	0.67	0.87	0.96	1.00	1.00	1.00	1.00

Table 7-8 and Appendix Tables E-4 through E-6 provide the same information on power as Table 7-7 and Appendix Tables E-1 through E-3 for a continuous dependent variable at a significance level of 0.05. The power calculations are defined in terms of the coefficient of variation (100 times the standard deviation of the dependent variable divided by the mean of the dependent variable) and the proportion mean change. The coefficient of variation relates the spread of the data relative to the magnitude of the data. In general, the power of a test is greater when the coefficient of variation is smaller. Table 7-8 presents power calculations for Model 1 (group), and Appendix Tables E-4 through E-6 present power calculations for Model 2 (initial dioxin), Model 3 (categorized dioxin—low plus high Ranch Hand versus Comparison contrast) and Model 4 (lipid-adjusted 1987 dioxin). Power calculations were performed using the logarithm (base 2) of dioxin in Models 2 and 4, and consequently, the relative risk is for a twofold increase in dioxin. The power of a test for a continuous variable depends on the significance level, actual difference in the true dependent variable means or slope of the dioxin coefficient, variation in the dependent variable data, sample size, and the distribution of the dioxin data if dioxin is the exposure estimate.

The proportion mean change in Table 7-8 and Appendix Table E-5 is defined as the difference in the true Ranch Hand and Comparison means, relative to the combined average of the two groups, assuming no transformation of the dependent variable. The proportion mean change in Appendix Tables E-4 and E-6 is defined as the change in the expected value (mean) of the dependent variable for a twofold increase in initial dioxin, relative to the dependent variable mean. The proportion mean change in Appendix Tables E-4 and E-6 corresponds mathematically to the slope of initial or 1987 dioxin divided by the dependent variable mean, assuming no transformation of the dependent variable. Analogous quantities can be derived based on transformed statistics. As an example, white blood cell count (on the natural logarithm scale) for all participants has a coefficient of variation of approximately 15 percent. With this coefficient of variation, for the 870 Ranch Hands and 1,251 Comparisons in Model 1, the power is approximately 0.86 for detecting a 2-percent increase in the mean white blood cell count of Ranch Hands relative to the mean white blood cell count of Comparisons (mean change = 0.02).

Table 7-8. Approximate Power To Detect a Group Effect at a 5-Percent Level of Significance (Continuous Dependent Variable)

	Coefficient of Variation ($100\sigma/\mu$)					
Mean Change	5	10	15	25	50	75
0.005	0.62	0.21	0.12	0.07	0.06	0.05
0.01	0.99	0.62	0.33	0.15	0.08	0.06
0.02	1.00	0.99	0.86	0.44	0.15	0.09
0.03	1.00	1.00	0.99	0.78	0.27	0.15
0.04	1.00	1.00	1.00	0.95	0.44	0.23
0.05	1.00	1.00	1.00	0.99	0.62	0.33
0.10	1.00	1.00	1.00	1.00	0.99	0.86

In summary, this study has good power to detect relative risks of 2.0 or more with respect to diseases, such as heart disease and basal cell carcinoma, occurring at a prevalence of at least 5 percent in unexposed populations. In addition, the study size is sufficient to detect small mean shifts in the continuously distributed variables. The detection of significant mean shifts without a corresponding indication of increased Ranch Hand abnormalities or disease may be an artifact of multiple testing, could represent a subclinical effect, or could be of little or no medical importance.

7.6 EXPLANATION OF TABLES

This section explains the contents of the tables used to report the results of the analyses for continuous and discrete dependent variables (two levels and more than two levels). Selected tables from the General Health Assessment (Chapter 9) and the Hematology Assessment (Chapter 15) will be referenced throughout this discussion. The contents of each table depend on the form of the health status endpoint (i.e., whether the dependent variable under analysis is a continuous or discrete variable). A discussion of the contents of exposure analysis tables is discussed first, followed by an explanation of the longitudinal analysis tables.

7.6.1 Exposure Analysis

The results of the exposure analysis are displayed in subpanels within each table as specified in Table 7-9. The specification of the subpanels is applicable whether the dependent variable is continuous or discrete.

Table 7-9. Location of Table Results from Different Exposure Analysis Models

Model	Exposure Estimate	Subpanel in Table	Type of Analysis
1	Group[a]	a	Unadjusted
		b	Adjusted
2	Initial Dioxin[b]	c	Unadjusted
		d	Adjusted
3	Categorized Dioxin[a]	e	Unadjusted
		f	Adjusted
4	1987 Dioxin[b]	g	Unadjusted
		h	Adjusted

[a] Ranch Hands and Comparisons.
[b] Ranch Hands only.

7.6.1.1 Continuous Variables

Table 9-8 in the General Health Assessment chapter presents an example of the results of the analysis when the dependent variable was continuous. Subpanels (a) and (b) show the results of unadjusted and adjusted Model 1 analyses that compared the Ranch Hand and Comparison means of a dependent variable. Contrasts between Ranch Hands and Comparisons also are presented within each occupational category (i.e., officer, enlisted flyer, and enlisted groundcrew).

For the unadjusted analysis in subpanel (a), a sample size (n) and a mean are presented for all occupational categories combined and separately for each occupational category. If the dependent variable was transformed for the analysis, the means of the transformed values were converted to the original scale and the column heading is footnoted. For each contrast of Ranch Hands versus Comparisons, the difference of means on the original scale and the associated 95-percent confidence interval are reported. The 95-percent confidence interval was constructed by adding and subtracting 1.96 multiplied by the standard error (for the upper and lower bounds, respectively) to the estimated mean. If the analysis was performed on a transformed scale, the 95-percent confidence interval on the differences of means is not presented and the column is footnoted. When presenting results from analyses of means based on log-transformed (or square root-transformed) data, means were converted back to original units. Conversion of the standard deviation from log units to original units is not recommended (25); therefore, confidence intervals for mean differences in original units are not presented. A p-value also is reported to determine whether a difference in means on the scale used for analysis for a specified contrast was equal to zero. The confidence interval and p-value for each occupational category were determined using analysis of variance techniques from a group-by-occupation interaction in the model. The group-by-occupation interaction was used to determine the model coefficients and standard errors simultaneously for officers, enlisted flyers, and enlisted groundcrew. The respective coefficients and standard errors from the group and group-by-interaction terms in the model, along with the covariances between the estimates, were combined as appropriate to construct the confidence intervals and p-values for the three occupational strata.

For an adjusted Model 1 analysis, subpanel (b) includes a sample size, an adjusted mean, a difference of Ranch Hand and Comparison adjusted means on the original scale, the associated 95-percent confidence interval (if the analysis was performed on the original scale), and a p-value for each contrast. Sample sizes for corresponding panels of unadjusted and adjusted analyses may differ because of missing covariate information. The confidence interval and p-value for each occupational category were determined using analysis of covariance techniques from a group-by-occupation interaction in the model.

Subpanel (c) of Table 9-8 reports summary statistics from the analysis that assessed the association between the continuous dependent variable and initial dioxin (Model 2) without adjusting for covariate information. The sample size and mean of the dependent variable (transformed to the original units, if necessary) are presented for low, medium, and high categories of initial dioxin. The low, medium, and high categories were determined by dividing all Ranch Hands with initial dioxin estimates into three approximately equal-sized categories based on their initial dioxin estimate. The numerical values defining these categories are specified in a table subpanel footnote. Means of the dependent variable, adjusted for percent body fat at the time of the blood measurement of dioxin, also are presented for the low, medium, and high categories of initial dioxin. Based on a linear regression analysis, adjusted for percent body fat at the time of the blood measurement of dioxin, the coefficient of determination (R^2), the estimated slope, and its associated standard error are reported. If the dependent variable was transformed for the regression analysis, the transformation is identified in the footnote. The p-value associated with testing whether the slope was equal to zero also is presented. The summary statistics that are reported were based on initial dioxin divided into three categories, whereas the R^2, slope, standard error, and p-value were based on $\log_2$ (initial dioxin) in its continuous form.

Based on analyses that incorporate covariate information, subpanel (d) reports summary statistics from the analysis that assessed the association between the continuous dependent variable and initial dioxin (Model 2). Similar to the unadjusted analysis, a sample size and adjusted mean of the dependent variable (transformed to the original units, if necessary) are presented for low, medium, and high categories of initial dioxin. The numerical values defining these categories are specified in a table subpanel footnote.

Sample sizes for corresponding panels of unadjusted and adjusted analyses may differ because of missing covariate information. Based on the multiple linear regression of the dependent variable on $\log_2$ (initial dioxin) and covariate effects, including percent body fat at the time of the blood measurement of dioxin, the coefficient of determination (R^2), the adjusted slope for $\log_2$ (initial dioxin), and its associated standard error are reported. If the dependent variable was transformed for the regression analysis, the adjusted means, adjusted slope, and standard error are footnoted and the transformation is identified in the footnote. The p-value for testing whether the slope was equal to zero also is presented.

Subpanels (e) and (f) of Table 9-8 show the results of unadjusted and adjusted Model 3 analyses that contrasted the means of a continuous dependent variable for Ranch Hands with background, low, high, and low plus high dioxin levels with Comparisons having lipid-adjusted dioxin levels less than or equal to 10 ppt. The low and high Ranch Hand categories were determined by dividing all Ranch Hands with lipid-adjusted dioxin estimates greater than 10 ppt into two approximately equal-sized categories based on their initial dioxin estimate. The low plus high Ranch Hand category is a combination of the low and high categories. The note at the bottom of the table subpanels defines the dioxin categories. The mean for the low plus high category is a weighted average (transformed to the original units, if necessary) of the low Ranch Hand and high Ranch Hand categories' means on the scale used for transformation, where the weights were based on the low and high Ranch Hand categories' sample sizes. Sample sizes for corresponding panels of unadjusted and adjusted analyses may differ because of missing covariate information.

For the unadjusted analysis in subpanel (e), a sample size and dependent variable mean are presented for each category. If the dependent variable was transformed for the analysis, the means of the transformed values were converted to the original scale and the column heading is footnoted. The mean of the dependent variable adjusted for percent body fat at the time of the blood measurement of dioxin also is presented for each dioxin category. For each individual contrast of the Ranch Hand category versus the Comparison category, the difference of means on the original scale and the associated 95-percent confidence interval are reported. If the analysis was performed on a transformed scale, the 95-percent confidence interval on the differences of means is not presented and the column is footnoted. A p-value also is reported to determine whether a difference in means for a specified contrast was equal to zero. The p-value was based on the difference of means on the scale used for analysis. The adjusted mean, confidence interval, and p-value for each contrast was determined from an analysis of covariance model with adjustment for percent body fat at the time of the blood measurement of dioxin.

For the adjusted analysis in subpanel (f), the table includes a sample size, an adjusted mean (adjusted for percent body fat at the time of the blood measurement of dioxin and covariates), a difference in adjusted means on the original scale, and a 95-percent confidence interval on the difference in adjusted means (if the analysis was performed on the original scale). The p-value for testing whether the difference in adjusted means for a specified contrast was equal to zero also is presented.

Subpanel (g) of Table 9-8 reports summary statistics from Model 4 analyses, which assessed the association between the continuous dependent variable and 1987 dioxin without adjusting for covariate information. The sample size and mean of the dependent variable (transformed to the original units, if necessary) are presented for low, medium, and high categories of 1987 dioxin. The low, medium, and high categories were determined by dividing all Ranch Hands with 1987 dioxin levels into three approximately equal-sized categories based on their 1987 dioxin measurement. The numerical values defining the low, medium, and high categories of 1987 dioxin are specified in a table subpanel footnote. Based on a linear regression of the dependent variable on $\log_2$ (1987 dioxin + 1), the coefficient of determination (R^2), the estimated slope, and its associated standard error are reported for each model. A

value of 1 was added to each measurement because of the presence of 1987 dioxin measurements of 0 ppt. If the dependent variable was transformed for the regression analysis, the means, slope, and standard error are footnoted and the transformation is identified in the footnote. The p-value associated with testing whether the slope was equal to zero also is presented.

Based on analyses that incorporate covariate information, subpanel (h) reports summary statistics for Model 4 analyses that assessed the association between the continuous dependent variable and 1987 dioxin. The sample size and adjusted mean of the dependent variable (transformed to the original units, if necessary) are presented for low, medium, and high categories of 1987 dioxin. The numerical values defining these categories are specified in a table subpanel footnote. Sample sizes for corresponding panels of unadjusted and adjusted analyses may differ because of missing covariate information. Based on the multiple linear regression of the dependent variable on $\log_2$ (1987 dioxin + 1) and covariates, the coefficient of determination (R^2), the adjusted slope for $\log_2$ (1987 dioxin + 1), and its associated standard error are reported for each model. If the dependent variable was transformed for the regression analysis, the adjusted means, adjusted slope, and standard error are footnoted and the transformation is identified in the footnote. The p-value for testing whether the slope was equal to zero also is presented.

7.6.1.2 Discrete Variables

7.6.1.2.1 Discrete Variable with Two Categories

Table 9-3 in the General Health Assessment chapter presents an example of the results of analysis when the dependent variable is discrete and dichotomous. Subpanels (a) and (b) display the results of unadjusted and adjusted Model 1 analyses that compared the percentage of Ranch Hands and Comparisons that were considered abnormal for the dependent variable of interest (the abnormal classification for self-perception of health in Table 9-3 is "fair or poor"). Contrasts between Ranch Hands and Comparisons also are presented within each occupational category (i.e., officer, enlisted flyer, and enlisted groundcrew). For the unadjusted analysis in subpanel (a), a sample size and the number and percentage of participants considered abnormal are presented for each group within each occupational category. For the contrasts of Ranch Hands versus Comparisons, an estimated relative risk, an associated 95-percent confidence interval on the relative risk, and a p-value for testing whether the risk was equal to 1.0 are presented. The normal distribution was used to calculate an approximate 95-percent confidence interval. Results for each occupational category were determined from a group-by-occupation interaction that was included in the model.

For the adjusted analysis of Model 1, as presented in subpanel (b), the table presents an adjusted relative risk, a 95-percent confidence interval on the relative risk, and a p-value for testing whether the risk was equal to 1.0. The adjusted relative risk, confidence interval, and p-value were determined from a multiple logistic regression model that used the appropriate covariates for the clinical area and dependent variable of interest. Results for each occupational category were determined from a group-by-occupation interaction that was included in the model.

Subpanel (c) of Table 9-3 reports summary statistics for analyses that assessed the association between the dependent variable and initial dioxin (Model 2) without adjusting for covariate information. Sample sizes are presented for low, medium, and high categories of initial dioxin. The numerical values defining these categories are specified in a table footnote. The number and percentage of Ranch Hands considered abnormal are presented for the low, medium, and high initial dioxin categories. Based on a logistic regression model, adjusted for percent body fat at the time of the blood measurement of dioxin, an estimated relative risk and its 95-percent confidence interval are reported. The p-value associated

with testing whether the relative risk was equal to 1.0 also is presented. The normal distribution was used to determine an approximate 95-percent confidence interval. The summary statistics that are reported were based on initial dioxin divided into three categories, whereas the relative risk, confidence interval, and p-value were based on $\log_2$ (initial dioxin) in its continuous form.

Subpanel (d) of Table 9-3 reports summary statistics for analyses that assessed the association between the discrete dependent variable and initial dioxin (Model 2), adjusted for percent body fat at the time of the blood measurement of dioxin and covariate information. The sample size given is based on a multiple logistic regression of the discrete dependent variable on $\log_2$ (initial dioxin), percent body fat at the time of the blood measurement of dioxin, and covariates. Sample sizes for corresponding panels of unadjusted and adjusted analyses may differ because of missing covariate information. The adjusted relative risk for $\log_2$ (initial dioxin) and its associated 95-percent confidence interval are reported and are based on this multiple logistic regression model. The normal distribution was used to determine an approximate 95-percent confidence interval. The p-value for testing whether the relative risk was equal to 1.0 also is presented.

Subpanels (e) and (f) of Table 9-3 show the results of unadjusted and adjusted Model 3 analyses that contrasted Ranch Hands having background, low, high, and low plus high dioxin levels with Comparisons having lipid-adjusted dioxin levels less than or equal to 10 ppt. The percentage of participants that were considered abnormal for the dependent variable of interest was contrasted between the four categories of Ranch Hands and Comparisons. The low and high Ranch Hand categories were determined by dividing all Ranch Hands with lipid-adjusted dioxin estimates greater than 10 ppt into two approximately equal-sized categories based on their initial dioxin estimate. The low plus high Ranch Hand category is a combination of the low and high Ranch Hand categories. The note at the bottom of the table subpanel defines the dioxin categories. The percentage of Ranch Hands in the low plus high category is a weighted average of the low Ranch Hand and high Ranch Hand categories, where the weights are based on the low category and high category sample sizes. Sample sizes for corresponding panels of unadjusted and adjusted analyses may differ because of missing covariate information.

For the Model 3 unadjusted analysis in subpanel (e), the sample size and the number and percentage of participants considered abnormal is presented for each dioxin category. For the individual contrasts of the Ranch Hand categories versus Comparisons, an estimated relative risk, a 95-percent confidence interval for the relative risk, and a p-value associated with testing whether the risk was equal to 1.0 are presented. The relative risk, confidence interval, and p-value were determined from a logistic regression model, adjusted for percent body fat at the time of the blood measurement of dioxin. The normal distribution was used to determine an approximate 95-percent confidence interval.

For the Model 3 adjusted analysis, subpanel (f) of the table presents an adjusted relative risk, a 95-percent confidence interval for the relative risk, and a p-value associated with testing whether the risk was equal to 1.0 for the individual contrasts of the Ranch Hand categories with Comparisons. The normal distribution was used to determine an approximate 95-percent confidence interval.

Subpanels (g) and (h) of Table 9-3 present summary statistics from Model 4, which assessed the association between the dependent variable and 1987 dioxin. For the unadjusted analysis, the sample size and the number and percentage of participants considered abnormal is presented for each 1987 dioxin category. The low, medium, and high categories were determined by dividing all Ranch Hands with 1987 dioxin levels into three approximately equal-sized categories. The numerical values defining these categories are specified in a table footnote. Based on a logistic regression model, an estimated relative risk and its 95-percent confidence interval are reported. The p-value associated with testing

whether the relative risk was equal to 1.0 also is presented. The normal distribution was used to determine an approximate 95-percent confidence interval. The summary statistics are reported for 1987 dioxin divided into three categories, whereas the relative risk, confidence interval, and p-value were based on $\log_2$ (1987 dioxin + 1) in its continuous form.

Incorporating covariate information, subpanel (h) reports summary statistics from analyses that assessed the association between the dichotomous dependent variable and 1987 dioxin. The sample size is presented for a multiple logistic regression of the discrete dependent variable on $\log_2$ (1987 dioxin + 1) including covariates in the final adjusted model. Sample sizes for corresponding panels of unadjusted and adjusted analyses may differ because of missing covariate information. Based on the multiple logistic regression model, the adjusted relative risk for $\log_2$ (1987 dioxin + 1) and its associated 95-percent confidence interval are reported. The normal distribution was used to determine an approximate 95-percent confidence interval. The p-value for testing whether the relative risk was equal to 1.0 also is presented.

7.6.1.2.2 Discrete Variable with More Than Two Categories

Polytomous regression techniques were used to analyze discrete dependent variables having more than two levels (e.g., abnormal low, normal, abnormal high—see Table 15-4 in the Hematology Assessment chapter). Results were presented in a similar fashion to discrete variables with only two categories; however, the number and percentage of participants for each dependent variable category (including normal) are given. Therefore, the relative frequencies sum to 100 percent across the dependent variable categories and the number of participants in each of the dependent variable categories adds to the total number of participants in each exposure group or dioxin category. In addition, a relative risk, a 95-percent confidence interval, and a p-value were presented for each contrast with the normal level of the dependent variable (e.g., abnormal low versus normal and abnormal high versus normal).

In Table 15-4, subpanels (a) and (b) display the results of unadjusted and adjusted Model 1 analyses that compared Ranch Hands and Comparisons on the relative frequencies of each abnormal level for a specified discrete dependent variable. For example, the percentage of participants with an abnormally high red blood cell count was contrasted to participants with a normal red blood cell count, and the percentage of participants with an abnormally low red blood cell count was contrasted to participants with a normal red blood cell count. Contrasts between Ranch Hands and Comparisons also are presented within each occupational category (i.e., officer, enlisted flyer, and enlisted groundcrew). For the unadjusted analysis in subpanel (a), a sample size is presented for each exposure group (Ranch Hand, Comparison) across all occupational categories and within each occupational category. The number and percentage of participants are presented for each level of the dependent variable for each group. For the contrasts of Ranch Hands versus Comparisons, an estimated relative risk, a 95-percent confidence interval for the relative risk, and a p-value associated with testing whether the risk was equal to 1.0 are presented for each contrast against the normal level of the dependent variable (e.g., abnormal low versus normal and abnormal high versus normal). The normal distribution was used to calculate an approximate 95-percent confidence interval. Results for each occupational category were determined from the group-by-occupation interaction that was included in the model.

For a Model 1 analysis adjusted for covariate information and shown in subpanel (b), the table presents an adjusted relative risk, a 95-percent confidence interval on the relative risk, and a p-value associated with testing whether the risk was equal to 1.0 for each occupational category and each contrast. The normal distribution was used to calculate an approximate 95-percent confidence interval. Results for

each occupational category were determined from the group-by-occupation interaction that was included in the model.

Subpanels (c) and (d) of Table 15-4 summarize the unadjusted and adjusted Model 2 analyses relating discrete dependent variables having more than two categories to initial dioxin. Both unadjusted and adjusted analyses are adjusted for percent body fat at the time of the blood measurement of dioxin. In subpanel (c), the sample size and the number and percentage of Ranch Hands in each category of the dependent variable are presented for each initial dioxin category (i.e., low, medium, and high initial dioxin). The relative risk, the 95-percent confidence interval for the relative risk, and the p-value associated with testing whether the risk was equal to 1.0 are presented for each abnormal level of the dependent variable (e.g., abnormal low versus normal and abnormal high versus normal). The summary statistics that are reported were based on initial dioxin divided into three categories, whereas the relative risk, confidence interval, and p-value were based on $\log_2$ (initial dioxin) in its continuous form.

In subpanel (d), after adjustment for covariate information, the sample size, the adjusted relative risk, the 95-percent confidence interval for the relative risk, and the p-value associated with testing whether the risk was equal to 1.0 are presented for each abnormal level of the dependent variable. Sample sizes for corresponding panels of unadjusted and adjusted analyses may differ because of missing covariate information.

Subpanels (e) and (f) of Table 15-4 present unadjusted and adjusted Model 3 analyses of categorized dioxin versus a discrete dependent variable having more than two categories. Both unadjusted and adjusted analyses are adjusted for percent body fat at the time of the blood measurement of dioxin. Results are presented in a similar fashion to the group analysis (Model 1), except that contrasts involve the four Ranch Hand categories (background, low, high, and low plus high) versus Comparisons, and contrasts are not performed for each occupation. For the unadjusted analysis, a sample size is presented for each dioxin category. The low plus high Ranch Hand category is a combination of the low and high Ranch Hand categories. The percentage of Ranch Hands in the low plus high category is a weighted average of the low Ranch Hand and high Ranch Hand categories, where the weights are based on the low category and high category sample sizes. Sample sizes for corresponding panels of unadjusted and adjusted analyses may differ because of missing covariate information.

The number and percentage of participants for each level of the dependent variable are presented for each dioxin category in subpanel (e). For each contrast of a Ranch Hand category versus the Comparison group, an estimated relative risk, a 95-percent confidence interval for the relative risk, and a p-value associated with testing whether the risk was equal to 1.0 are presented. These results are given for each contrast against the normal level of the dependent variable (e.g., abnormal low versus normal and abnormal high versus normal). For an adjusted Model 3 analysis in subpanel (f), the table presents an adjusted relative risk, a 95-percent confidence interval on the relative risk, and a p-value for each contrast of Ranch Hands versus Comparisons for each abnormal level of the dependent variable.

Similar to the polytomous regression analysis using initial dioxin, unadjusted and adjusted analyses of discrete dependent variables with more than two categories were performed using 1987 dioxin in Model 4. In Table 15-4, summaries of the analyses are given in subpanels (g) and (h). For the unadjusted analysis in subpanel (g), sample sizes are presented for each 1987 dioxin category (i.e., low, medium, and high 1987 dioxin). The number and percentage of Ranch Hands for each dependent variable category for each 1987 dioxin category are presented. An estimated relative risk, a 95-percent confidence interval on the relative risk, and an associated contrast p-value are reported for each abnormal level of the dependent variable (e.g., abnormal low vs. normal and abnormal high vs. normal). The summary statistics that are

reported were based on 1987 dioxin divided into three categories, whereas the relative risk, confidence interval, and p-value were based on $\log_2$ (1987 dioxin + 1) in its continuous form.

Adjusted analysis results in subpanel (h) include a total sample size, an adjusted relative risk, a 95-percent confidence interval on the relative risk, and an associated contrast p-value for each abnormal level of the dependent variable. Sample sizes for corresponding panels of unadjusted and adjusted analyses may differ because of missing covariate information.

7.6.2 Longitudinal Analysis

The results of the longitudinal analysis are displayed in subpanels within each table as specified in Table 7-10. The specification of the subpanels is applicable whether the dependent variable is continuous or discrete.

Table 7-10. Location of Table Results from Different Longitudinal Analysis Models

Model	Exposure Estimate	Subpanel in Table
1	Group[a]	a
2	Initial Dioxin[b]	b
3	Categorized Dioxin[a]	c

[a] Ranch Hands and Comparisons.
[b] Ranch Hands only.

Most of the longitudinal analyses in this report are based on a comparison of data from the 1982 baseline examination and the 1997 follow-up examination, and the discussion of tables below is based on the comparison of the 1982 and 1997 examinations. Some analyses, however, are based on a comparison of data from the 1985 follow-up examination and the 1997 follow-up examination (e.g., neurological indices in Chapter 11, Neurological Assessment, or Doppler pulses in Chapter 14, Cardiovascular Assessment). The 1985 follow-up examination data were used because of methodological differences in the measurements between the 1982 baseline examination and the 1985 follow-up examination, or because the measurement was not obtained at the 1982 baseline examination. In addition, spirometry measurements were not taken at the 1985 follow-up examination, and Doppler pulse measurements were not made at the 1987 follow-up examination; therefore, summary statistics based on data from the respective examinations are not provided for these variables.

7.6.2.1 Continuous Variables

Table 9-15 in the General Health Assessment chapter presents an example of a longitudinal analysis when the dependent variable was continuous. In subpanel (a), a mean and a sample size (n) are provided for all occupational categories combined and separately for each occupational category (i.e., officer, enlisted flyer, and enlisted groundcrew). The mean and sample size are provided for data from the 1982 baseline examination and the 1985, 1987, 1992, and 1997 follow-up examinations. Summary statistics for the 1982 baseline examination and the 1997 follow-up examination were based on participants that attended both examinations. Summary statistics for the 1985, 1987, and 1992 follow-up examinations were based on participants that attended the 1982 baseline examination, the 1997 follow-up examination,

and the respective follow-up examination that was summarized. The summary statistics for the 1985, 1987, and 1992 follow-up examinations are provided for reference purposes. If the dependent variable was transformed for the analysis, the means of the transformed values were converted to the original scale and the transformation is specified in a footnote.

Subpanel (a) shows the Ranch Hand and Comparison difference in means between the 1997 follow-up examination and 1982 baseline examination. The Ranch Hand and Comparison difference in means between the 1997 follow-up examination and 1982 baseline examination is presented for all occupations combined and separately for each occupational category. The difference between Ranch Hands and Comparisons in the change between the 1997 follow-up examination mean and the 1982 baseline examination mean also is reported in subpanel (a). The p-value that was used to determine whether the difference in the examination mean change between Ranch Hands and Comparisons was equal to zero is given. This p-value was based on the difference in Ranch Hand and Comparison examination mean changes on the scale used for analysis. The p-value for each occupational category was determined using analysis of covariance techniques from a group-by-occupation interaction in the model. The longitudinal analysis performed in subpanel (a) was adjusted for the 1982 measurement of the dependent variable and age at the 1997 physical examination.

Subpanel (b) of Table 9-15 reports summary statistics on the continuous dependent variable of interest. The sample size and mean of the dependent variable (transformed to the original units, if necessary) are presented for low, medium, and high categories of initial dioxin. The low, medium, and high categories were determined by dividing all Ranch Hands with initial dioxin estimates into three approximately equal-sized categories based on their initial dioxin estimate. The numerical values defining these categories are specified in the table subpanel footnote. The mean and sample size are provided for data from the 1982 baseline examination and the 1985, 1987, 1992, and 1997 follow-up examinations. Summary statistics for the 1982 baseline examination and the 1997 follow-up examination were based on participants that attended both examinations. Summary statistics for the 1985, 1987, and 1992 follow-up examinations were based on participants that attended the 1982 baseline examination, the 1997 follow-up examination, and the respective follow-up examination that was summarized. If the dependent variable was transformed for the analysis, the transformation is specified in a footnote.

For each participant who attended both the 1982 and 1997 physical examinations, a difference between the dependent variable as measured at the 1997 follow-up examination and as measured at the 1982 baseline examination was created. The difference in these two measurements was on the scale used for analysis. The association between the difference in the examination measurements and initial dioxin was determined and adjusted for the 1982 measurement of the dependent variable, age at the 1997 physical examination, and percent body fat at the time of the blood measurement of dioxin. The estimated slope, its associated standard error, and the p-value associated with testing whether the slope was equal to zero are reported in subpanel (b). If the dependent variable was transformed for the regression analysis, the transformation is identified in the footnote. The summary statistics that are reported were based on initial dioxin divided into three categories, whereas the slope, standard error, and p-value were based on $\log_2$ (initial dioxin) in its continuous form.

Subpanel (c) of Table 9-15 shows the results of Model 3 analyses that contrasted the means of a continuous dependent variable for Ranch Hands with background, low, high, and low plus high dioxin levels with Comparisons having lipid-adjusted dioxin levels less than or equal to 10 ppt. The low and high Ranch Hand categories were determined by dividing all Ranch Hands with lipid-adjusted dioxin estimates greater than 10 ppt into two approximately equal-sized categories based on their initial dioxin estimate. The low plus high Ranch Hand category is a combination of the low and high categories. The

note at the bottom of the table subpanel defines the dioxin categories. The mean for the low plus high category is a weighted average (transformed to the original units, if necessary) of the low Ranch Hand and high Ranch Hand category means on the scale used for transformation, where the weights were based on the low and high Ranch Hand category sample sizes.

In subpanel (c), a mean and a sample size are provided for all Ranch Hand and Comparison dioxin categories. The mean and sample size are provided for data from the 1982 baseline examination and the 1985, 1987, 1992, and 1997 follow-up examinations. Summary statistics for the 1982 baseline examination and the 1997 follow-up examination were based on participants that attended the 1982 baseline examination and the 1997 follow-up examination. Summary statistics for the 1985, 1987, and 1992 follow-up examinations were based on participants that attended the 1982 baseline examination, the 1997 follow-up examination, and the respective follow-up examination that was summarized. The summary statistics for the 1985, 1987, and 1992 follow-up examinations are provided for reference purposes. If the dependent variable was transformed for the analysis, the means of the transformed values were converted to the original scale and the transformation is specified in a footnote.

Subpanel (c) shows the Ranch Hand and Comparison difference in dioxin category means between the 1997 follow-up examination and 1982 baseline examination. The Ranch Hand and Comparison difference in dioxin category means between the 1997 follow-up examination and 1982 baseline examination is presented for all occupations combined and separately for each occupational category. The difference between Ranch Hands and Comparisons in the change between the 1997 follow-up examination mean and the 1982 baseline examination mean also is reported in subpanel (c). The p-value that was used to determine whether the difference in the examination mean change between the Ranch Hand dioxin category and Comparisons was equal to zero is given. This p-value was based on the difference in Ranch Hand and Comparison examination mean changes on the scale used for analysis. The p-value for each occupational category was determined using analysis of covariance techniques. The longitudinal analysis performed in subpanel (c) was adjusted for the 1982 measurement of the dependent variable, age at the 1997 physical examination, and percent body fat at the time of the blood measurement of dioxin.

7.6.2.2 Discrete Variables with Two Categories

Table 9-10 in the General Health Assessment chapter presents an example of the longitudinal analysis when the dependent variable was discrete and dichotomous. In subpanel (a), the number and percentage of participants defined as abnormal and a sample size (n) are provided for all occupational categories combined and separately for each occupational category (i.e., officer, enlisted flyer, and enlisted groundcrew). The summary statistics are provided for data from the 1982 baseline examination and the 1985, 1987, 1992, and 1997 follow-up examinations. Summary statistics for the 1982 baseline examination and the 1997 follow-up examination were based on participants that attended both examinations. Summary statistics for the 1985, 1987, and 1992 follow-up examinations were based on participants that attended the 1982 baseline examination, the 1997 follow-up examination, and the respective follow-up examination that was summarized. The summary statistics for the 1985, 1987, and 1992 follow-up examinations are provided for reference purposes.

Subpanel (a) also shows the number of Ranch Hands and Comparisons and the number and percentage of participants considered abnormal at the 1997 examination (the abnormal classification for self-perception of health in Table 9-10 is "fair or poor"). These summary statistics are presented for all occupations combined and separately for each occupational category, and are restricted to participants that were considered normal in 1982 (the normal classification for self-perception of health in Table 9-10 is

"excellent or good"). For the contrasts of Ranch Hands versus Comparisons, a relative risk, an associated 95 percent confidence interval on the relative risk, and a p-value for testing whether the risk was equal to 1.0 are presented. The normal distribution was used to calculate an approximate 95-percent confidence interval. Results for each occupational category were determined from the group-by-occupation interaction that was included in the logistic regression model. The longitudinal analysis performed in subpanel (a) was adjusted for age at the 1997 physical examination.

Subpanel (b) of Table 9-10 reports the number and percentage of participants defined as abnormal and a sample size for low, medium, and high categories of initial dioxin. The low, medium, and high categories were determined by dividing all Ranch Hands with initial dioxin estimates into three approximately equal-sized categories based on their initial dioxin estimate. The numerical values defining these categories are specified in the table subpanel footnote. The summary statistics are provided for data from the 1982 baseline examination and the 1985, 1987, 1992, and 1997 follow-up examinations. Summary statistics for the 1982 baseline examination and the 1997 follow-up examination were based on participants that attended both examinations. Summary statistics for the 1985, 1987, and 1992 follow-up examinations were based on participants that attended the 1982 baseline examination, the 1997 follow-up examination, and the respective follow-up examination that was summarized.

Based on a logistic regression model adjusted for age at the 1997 physical examination and percent body fat at the time of the blood measurement of dioxin, the association between the dichotomous dependent variable and initial dioxin was determined. The analysis was restricted to participants that were considered normal in 1982. The relative risk and its 95-percent confidence interval are reported in subpanel (b), along with the p-value associated with testing whether the relative risk was equal to 1.0. The summary statistics that are reported were based on initial dioxin divided into three categories, whereas the relative risk, confidence interval, and p-value were based on $\log_2$ (initial dioxin) in its continuous form.

Subpanel (c) of Table 9-10, for example, shows the sample size and the number and percentage of participants considered abnormal for Ranch Hands with background, low, high, and low plus high dioxin levels and Comparisons having lipid-adjusted dioxin levels less than or equal to 10 ppt. The low and high Ranch Hand categories were determined by dividing all Ranch Hands with lipid-adjusted dioxin estimates greater than 10 ppt into two approximately equal-sized categories based on their initial dioxin estimate. The low plus high Ranch Hand category is a combination of the low and high categories. The note at the bottom of the table subpanel defines the dioxin categories. The percentage of Ranch Hands in the low plus high category is a weighted average of the low Ranch Hand and high Ranch Hand categories, where the weights are based on the low category and high category sample sizes.

The summary statistics in subpanel (c) are provided for data from the 1982 baseline examination and the 1985, 1987, 1992, and 1997 follow-up examinations. Summary statistics for the 1982 baseline examination and the 1997 follow-up examination were based on participants that attended both examinations. Summary statistics for the 1985, 1987, and 1992 follow-up examinations were based on participants that attended the 1982 baseline examination, the 1997 follow-up examination, and the respective follow-up examination that was summarized.

Subpanel (c) also shows the number of Comparisons and Ranch Hands in each of the dioxin categories for the 1997 physical examination, and the number and percentage of participants considered abnormal at the 1997 examination. The analysis was restricted to participants that were considered normal in 1982. The relative risk and its 95-percent confidence interval are reported, along with the p-value associated with testing whether the relative risk was equal to 1.0. The normal distribution was used to calculate an

approximate 95-percent confidence interval. The longitudinal analysis was based on a logistic regression model and was adjusted for age at the 1997 physical examination and percent body fat at the time of the blood measurement of dioxin.

7.6.2.2.1 Discrete Variable with More Than Two Categories

An example of a longitudinal analysis on a discrete variable with more than two categories is provided in Table 15-26 in the Hematology Assessment chapter. The statistics provided in this table are identical to the statistics provided for a discrete variable with two categories (e.g., Table 9-10). The tables for a discrete variable with more than two categories have a separate subpanel for each abnormal level of the dependent variable. For example, in Table 15-26, platelet count has three levels: abnormal low, normal, and abnormal high. Subpanels (a1), (b1), and (c1) contrast abnormal low levels of platelet count with normal levels for Models 1, 2, and 3, respectively. Subpanels (a2), (b2), and (c2) contrast abnormal high levels of platelet count with normal levels for Models 1, 2, and 3, respectively. As with the longitudinal analysis on a dichotomous dependent variable, analyses are restricted to participants that were normal in 1982.

REFERENCES

1. Lathrop, G. D., W. H. Wolfe, R. A. Albanese, and P. M. Moynahan. 1984. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Baseline morbidity study results. NTIS: AD A 138 340. USAF School of Medicine, Brooks Air Force Base, Texas.

2. Lathrop, G. D., S. G. Machado, T. G. Karrison, W. D. Grubbs, W. F. Thomas, W. H. Wolfe, J. E. Michalek, J. C. Miner, and M. R. Peterson. 1987. Epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: First followup examination results. NTIS: AD A 188 262. USAF School of Medicine, Brooks Air Force Base, Texas.

3. Thomas, W. F., W. D. Grubbs, T. G. Karrison, M. B. Lustik, R. H. Roegner, D. E. Williams, W. H. Wolfe, J. E. Michalek, J. C. Miner, and R. W. Ogershok. 1990. An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: 1987 followup examination results, May 1987 to January 1990. NTIS: AD A 222 573. USAF School of Medicine, Brooks Air Force Base, Texas.

4. Grubbs, W. D., W. H. Wolfe, J. E. Michalek, D. E. Williams, M. B. Lustik, A. S. Brockman, S. C. Henderson, F. R. Burnett, R. G. Land, D. J. Osborne, V. K. Rocconi, M. E. Schreiber, J. C. Miner, G. L. Henriksen, and J. A. Swaby. 1995. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final Report. 1992 Followup Examination Results. NTIS: AD A 304 306, 304 308-316. USAF School of Medicine, Brooks Air Force Base, Texas.

5. Roegner, R. H., W. D. Grubbs, M. B. Lustik, A. S. Brockman, S. C. Henderson, D. E. Williams, W. H. Wolfe, J. E. Michalek, and J. C. Miner. 1991. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Serum Dioxin Analysis of 1987 Examination Results. NTIS: AD A 237 516-24. USAF School of Medicine, Brooks Air Force Base, Texas.

6. Lathrop, G. D., W. H. Wolfe, R. A. Albanese, and P. M. Moynahan. 1982. Epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Study Protocol. NTIS: AD A 122 250. USAF School of Aerospace Medicine, Brooks Air Force Base, Texas.

7. Michalek, J. E., J. L. Pirkle, S. P. Caudill, R. C. Tripathi, D. G. Patterson, and L. L. Needham. 1996. Pharmacokinetics of TCDD in veterans of Operation Ranch Hand: 10-year follow-up. *Journal of Toxicology and Environmental Health* 47:209-20.

8. Poiger, H., and C. Schalatter. 1986. Pharmacokinetics of 2,3,7,8-TCDD in man. *Chemosphere* 15:1489-94.

9. Kissel, J. C., and G. M. Robarge. 1988. Assessing the elimination of 2,3,7,8-TCDD from humans with a physiologically based pharmacokinetic model. *Chemosphere* 17:2017-27.

10. Akins, J. R., K. Waldrep, and J. T. Bernert Jr. 1989. The estimation of total serum lipids by a completely enzymatic "summation" method. *Clinica Chimica Acta* 184:219-26.

11. Patterson, D. G., L. Hampton, C. R. Lapeza, W. T. Belser, V. Green, L. Alexander, and L. Needham. 1987. High resolution gas chromatographic/high-resolution mass spectrometric analysis of human-serum on a whole-weight and lipid basis for 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Annals of Chemistry* 59:2000-5.

12. Patterson, D. G., L. L. Needham, J. L. Pirkle, D. W. Roberts, J. Bagby, W. A. Garret, J. S. Andrews Jr., H. Falk, J. T. Bernert, E. J. Sampson, and V. N. Houk. 1988. Correlation between serum and adipose tissue levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin in 50 persons from Missouri. *Archives of Environmental Toxicology* 17:139-43.

13. Knapik, J. J., A. R. L. Burse, and J. A. Vogel. 1983. Height, weight, percent body fat, and indices of adiposity for young men and women entering the Army. *Aviation, Space, and Environmental Medicine* 54:223-31.

14. *SAS/STAT User's Guide*. Version 6, 4th ed. 1990. Cary, North Carolina: SAS Institute, Inc.

15. *SAS/STAT software: Changes and enhancements through release 6.11*. 1996. Cary, North Carolina: SAS Institute, Inc.

16. Feinberg, S. E. 1981. *The analysis of cross-classified data*. Cambridge: MIT Press.

17. Bishop, Y. M. M., S. E. Feinberg, and P. W. Holland. 1975. *Discrete multivariate analysis: Theory and Practice*. Cambridge: MIT Press.

18. Neter, J., and W. Wasserman. 1974. *Applied linear statistical models*. Homewood, Illinois: Richard D. Irwin, Inc.

19. Cox, D. R. 1984. *Analysis of survival data*. London: Chapman and Hall.

20. Hosmer, D., and S. Lemeshow. 1989. *Applied logistic regression*. New York: John Wiley & Sons.

21. Agresti, A. 1990. *Categorical data analysis*. New York: John Wiley & Sons.

22. Mausner, J. S., and A. K. Bahn. 1974. *Epidemiology—An introductory text*. Philadelphia: W. B. Saunders Company.

23. Fleiss, J. L. 1986. *The design and analysis of clinical experiments*. New York: John Wiley & Sons.

24. Snedecor, G. W., and W. G. Cochran. 1980. *Statistical methods*. Ames, Iowa: The Iowa State University Press.

25. Steel, R. G. D., and J.H. Torrie. 1960. *Principles and Procedures of Statistics*. New York: McGraw-Hill Book Company, Inc.

Table of Contents

List of Tables

8 COVARIATE ASSOCIATIONS WITH ESTIMATES OF DIOXIN EXPOSURE

8.1 INTRODUCTION

The associations between the covariates used throughout this report and four estimates of dioxin exposure are evaluated in this chapter. The purpose of studying these associations was to determine if these covariates, which have been determined to be associated with one or more of the health endpoints considered in this study, were associated with an estimate of dioxin exposure, and, therefore, could potentially be confounding variables in subsequent statistical analyses in this report. These covariates and estimates of dioxin exposure are used extensively in the statistical analyses in Chapters 9 through 18. Specific definitions of the covariates are contained in these chapters. The results contained in this chapter are associations and should not be interpreted as indicating causal relations between the estimates of dioxin exposure and covariate levels.

In previous reports, the relations between the covariate and the estimates of dioxin exposure were not adjusted for other covariates, but some of the relations may have been confounded with military occupation. In this report, the unadjusted relations between dioxin exposure and all covariates were evaluated, as well as the relations when military occupation was considered. Consequently, for each association between a covariate and either group or dioxin, analyses unadjusted and adjusted for military occupation were performed.

Four models were examined for each covariate. Additional details regarding dioxin measurements are given in Chapter 2, Dioxin Assay, and Chapter 7, Statistical Methods. Model 1 examined the relation of an individual covariate with group (Ranch Hand or Comparison). In this model, exposure was defined as "yes" for Ranch Hands and "no" for Comparisons without regard to the magnitude of the exposure. Model 2 explored the relation between the covariate and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 parts per trillion (ppt). If a participant did not have a 1987 dioxin level, the 1992 level was used to estimate the initial dioxin level. If a participant did not have a 1987 or a 1992 dioxin level, the 1997 level was used to estimate the initial dioxin level.

Model 3 divided the Ranch Hands examined in Model 2 into two categories based on their initial dioxin measures. These two categories are referred to in the tables as "Low Ranch Hand" if the initial dioxin level was greater than 10 ppt and less than or equal to 94 ppt and "High Ranch Hand" if the initial dioxin level was greater than 94 ppt. Two additional categories, Ranch Hands with 1987 serum dioxin levels at or below 10 ppt and Comparisons with 1987 serum dioxin levels at or below 10 ppt, were created. Ranch Hands with 1987 serum dioxin levels at or below 10 ppt are referred to in the tables as the "Background Ranch Hand" category. Dioxin levels in 1992 were used if the 1987 level was not available, and dioxin levels in 1997 were used if the 1987 and 1992 levels were not available. Comparisons with 1987 dioxin levels greater than 10 ppt were excluded. Covariate means or covariate category percentages in the three Ranch Hand categories and the Comparison category were contrasted.

Model 4 examined the relation between the covariate and 1987 dioxin levels in all Ranch Hands with a dioxin measurement. If a participant did not have a 1987 dioxin measurement, the 1992 measurement was used in determining the dioxin level. If a participant did not have a 1987 or a 1992 dioxin measurement, the 1997 measurement was used in determining the dioxin level.

The summary statistics listed in the tables in this chapter are percentages, correlation coefficients (r), or means. For Models 1 and 3, if a covariate is discrete, the percentage of participants in each of the Ranch

Hand or Comparison categories is shown for each of the covariate categories. If a covariate is continuous, the mean of the covariate is given for each Ranch Hand and Comparison category. Because the measure of dioxin is continuous for the analyses of Models 2 and 4, if a covariate is also continuous, a correlation coefficient between initial dioxin and the covariate is provided. If a covariate is discrete, dioxin means for each of the covariate categories are displayed. Consistent with the methodology used in each of the clinical chapters, the means presented in the tables were transformed from the logarithmic (base 2) scale for initial dioxin in Model 2, and from the ($\log_2 (X+1)$) scale for 1987 dioxin in Model 4.

8.2 MATCHING DEMOGRAPHIC VARIABLES (AGE, RACE, AND MILITARY OCCUPATION)

Age, race, and military occupation were used in the design of the Air Force Health Study to match Ranch Hand participants with Comparisons to reduce the association between these variables and group status. It was impossible, however, to eliminate the possible confounding effect of these variables with serum dioxin in Models 2 through 4 through study design. Results of tests of association between age, race, and military occupation and the four estimates of dioxin exposure are given in Table 8-1.

Examining the association between age and dioxin revealed significant relations in the unadjusted analyses of Models 2, 3, and 4 for age in its continuous form ($p<0.001$ for each model). After adjusting for military occupation, however, the association was not significant in Models 2 or 4 ($p=0.266$ and $p=0.564$, respectively) but was significant in Model 3 ($p=0.016$). The highest mean age (60.0 years) was observed in the low Ranch Hand dioxin category, and youngest average age was observed for Ranch Hands in the high dioxin category, with a mean age of 55.8 years.

Dichotomized age (i.e., born before 1942, born in or after 1942) showed a significant relation ($p<0.001$) with dioxin exposure in Models 2, 3, and 4. When the relation was adjusted for military occupation, however, it was not significant in any of these models ($p>0.07$ for all three models).

Marginally significant unadjusted associations were observed between race and dioxin levels in Models 2 and 3 ($p=0.054$ and $p=0.089$, respectively). The unadjusted association in Model 4 was not significant ($p=0.587$). These effects were significant for Models 2, 3, and 4, however, when adjusting for military occupation ($p<0.001$, $p=0.015$, and $p=0.002$, respectively). Blacks had lower mean initial and 1987 dioxin levels than did non-Blacks in Models 2 and 4. In Model 3, the percentage of Blacks varied among Comparisons (5.8%), Ranch Hands in the background dioxin category (5.0%), Ranch Hands in the low dioxin category (9.6%), and Ranch Hands in the high dioxin category (5.4%).

Similar to the relation between age and dioxin, a significant association was found between military occupation and dioxin in Models 2, 3, and 4 ($p<0.001$ for each model). In Models 2 and 4, the mean dioxin levels were lowest among officers, followed by enlisted flyers and enlisted groundcrew. As expected, the percentages of officers, enlisted flyers, and enlisted groundcrew were similar between Ranch Hands and Comparisons in Model 1 ($p=0.302$), but the percentages varied considerably among the three Ranch Hand dioxin categories in Model 3. In Model 3, 61.4 percent of Ranch Hands in the background dioxin category were officers, but only 40.2 percent of Ranch Hands in the low dioxin category and 2.9 percent of Ranch Hands in the high dioxin category were officers.

Table 8-1. Associations Between Matching Demographic Variables (Age, Race, and Military Occupation) and Estimates of Herbicide or Dioxin Exposure

		Model 1				Model 2		
Covariate	Covariate Category	Ranch Hand Mean or n (%)	Comparison Mean or n (%)	p-Value: Unadjusted	p-Value: Adjusted[a]	Initial Dioxin (ppt) Correlation or Mean (n)	p-Value: Unadjusted	p-Value: Adjusted[a]
Age	n	870	1,251			482		
(continuous) (years)		$\bar{x}$ = 58.5	$\bar{x}$ = 58.4	0.677	0.924	r=–0.285	<0.001	0.266
(discrete)	Born <1942	495 (56.9)	693 (55.4)	0.522	0.745	$\bar{x}$ = 83.9 (n=250)	<0.001	0.075
	Born ≥1942	375 (43.1)	558 (44.6)			$\bar{x}$ = 144.9 (n=232)		
Race	n	870	1,251			482		
	Black	55 (6.3)	73 (5.8)	0.711	0.604	$\bar{x}$ = 82.3 (n=36)	0.054	<0.001
	Non-Black	815 (93.7)	1,178 (94.2)			$\bar{x}$ = 111.7 (n=446)		
Occupation	n	870	1,251			482		
	Officer	341 (39.2)	494 (39.5)	0.302	--	$\bar{x}$ = 50.0 (n=103)	<0.001	--
	Enlisted Flyer	151 (17.4)	187 (15.0)			$\bar{x}$ = 97.9 (n=103)		
	Enlisted Groundcrew	378 (43.5)	570 (45.6)			$\bar{x}$ = 152.1 (n=276)		

Table 8-1. Associations Between Matching Demographic Variables (Age, Race, and Military Occupation) and Estimates of Herbicide or Dioxin Exposure (Continued)

		Model 3					
Covariate	Covariate Category	Comparison Mean or n (%)	Background Ranch Hand Mean or n (%)	Low Ranch Hand Mean or n (%)	High Ranch Hand Mean or n (%)	p-Value: Unadjusted	p-Value: Adjusted[a]
Age	n	1,213	381	239	243		
(continuous) (years)		$\bar{x} = 58.4$	$\bar{x} = 59.4$	$\bar{x} = 60.0$	$\bar{x} = 55.8$	<0.001	0.016
(discrete)	Born <1942	671 (55.3)	242 (63.5)	155 (64.9)	95 (39.1)	<0.001	0.101
	Born ≥1942	542 (44.7)	139 (36.5)	84 (35.1)	148 (60.9)		
Race	n	1,213	381	239	243		
	Black	70 (5.8)	19 (5.0)	23 (9.6)	13 (5.4)	0.089	0.015
	Non-Black	1,143 (94.2)	362 (95.0)	216 (90.4)	230 (94.7)		
Occupation	n	1,213	381	239	243		
	Officer	478 (39.4)	234 (61.4)	96 (40.2)	7 (2.9)	<0.001	--
	Enlisted Flyer	185 (15.3)	48 (12.6)	51 (21.3)	52 (21.4)		
	Enlisted Groundcrew	550 (45.3)	99 (26.0)	92 (38.5)	184 (75.7)		

Table 8-1. Associations Between Matching Demographic Variables (Age, Race, and Military Occupation) and Estimates of Herbicide or Dioxin Exposure (Continued)

		Model 4		
Covariate	**Covariate Category**	**1987 Dioxin (ppt) Correlation or Mean (n)**	**p-Value: Unadjusted**	**p-Value: Adjusted[a]**
Age	n	863		
(continuous) (years)		r=–0.197	<0.001	0.564
(discrete)	Born <1942	$\bar{x}$ = 11.4 (n=492)	<0.001	0.542
	Born ≥1942	$\bar{x}$ = 18.2 (n=371)		
Race	n	863		
	Black	$\bar{x}$ = 12.9 (n=55)	0.587	0.002
	Non-Black	$\bar{x}$ = 14.1 (n=808)		
Occupation	n	863		
	Officer	$\bar{x}$ = 7.4 (n=337)	<0.001	--
	Enlisted Flyer	$\bar{x}$ = 15.4 (n=151)		
	Enlisted Groundcrew	$\bar{x}$ = 23.4 (n=375)		

[a] Adjusted for occupation.

Note: Means for discrete covariates were transformed from the logarithmic (base 2) scale for initial dioxin in Model 2 and from the ($\log_2$ (X+1)) scale for 1987 dioxin in Model 4.

8.3 ALCOHOL USE

Results of tests of association between alcohol use and the estimates of dioxin exposure are shown in Table 8-2. No significant association was found between dioxin and current alcohol use for Models 2, 3, and 4 using the discrete or the continuous form of alcohol use for unadjusted or adjusted analyses ($p>0.19$ for all analyses). Model 1 analyses showed a significant association between the discrete form of current alcohol use and group ($p=0.040$, unadjusted; $p=0.037$, adjusted). A greater percentage of Comparisons than Ranch Hands were light and heavy current drinkers (in terms of drinks per day), whereas a greater percentage of Ranch Hands than Comparisons were moderate current drinkers.

The adjusted and unadjusted associations between lifetime alcohol history and dioxin exposure were not significant in Models 1, 3, and 4 for either the continuous or discrete forms of alcohol history. Model 2 showed a significant association between lifetime alcohol history and initial dioxin in the adjusted model of the continuous form ($p=0.041$) and a marginally significant association with the discrete form ($p=0.078$).

Statistically significant and marginally significant associations were found in the unadjusted analysis of dioxin and current wine use for Model 2 ($p=0.038$, continuous; $p=0.004$, discrete), Model 3 ($p<0.001$ for both continuous and discrete), and Model 4 ($p<0.001$ for both continuous and discrete). None of these associations, however, was significant when the models were adjusted for military occupation ($p>0.63$ for all analyses).

Lifetime wine history, in the continuous form, differed significantly between Ranch Hands and Comparisons ($p=0.028$, unadjusted; $p=0.022$, adjusted for military occupation) and was marginally significant in the discrete form ($p=0.082$, unadjusted). Ranch Hands had a higher mean wine-years than Comparisons (3.86 wine-years vs. 3.03 wine-years), but a greater percentage of Comparisons than Ranch Hands (73.4% vs. 69.9%) had a history of wine use. Lifetime wine history showed significant inverse associations with dioxin in the unadjusted Model 2 ($p<0.001$ for continuous and discrete forms) and Model 4 ($p<0.001$ for continuous and discrete forms) analyses. When adjusting for military occupation, the associations between lifetime wine history and dioxin levels were no longer statistically significant ($p>0.12$ for all analyses). In Model 3, the unadjusted association between lifetime wine history and dioxin levels was significant ($p<0.001$ for the continuous and discrete forms of lifetime wine history). These results were marginally significant when adjusting for military occupation ($p=0.076$, continuous; $p=0.061$, discrete). The mean wine-years for Comparisons, Ranch Hands in the background dioxin category, Ranch Hands in the low dioxin category, and Ranch Hands in the high dioxin category for Model 3 were 3.07, 4.80, 4.55, and 1.73, respectively.

8.4 CIGARETTE SMOKING

Results of tests of association between cigarette smoking and the estimates of dioxin exposure are given in Table 8-3. No significant associations were observed between both current or lifetime cigarette smoking and group in Model 1 for adjusted or unadjusted analyses ($p>0.31$ for all analyses). No significant associations between the cigarette smoking covariates and initial dioxin were observed in Model 2 analyses ($p>0.20$ for all analyses). In Models 3 and 4, the unadjusted analyses showed no significant association between dioxin levels and current cigarette smoking or lifetime smoking habits ($p>0.17$ for all analyses); however, when adjusting for military occupation in Model 4, both the continuous and discrete forms of current and lifetime smoking showed significant associations with 1987

Table 8-2. Associations Between Alcohol Use and Estimates of Herbicide or Dioxin Exposure

Covariate	Covariate Category	Model 1: Ranch Hand Mean or n (%)	Model 1: Comparison Mean or n (%)	Model 1: p-Value: Unadjusted	Model 1: p-Value: Adjusted[a]	Model 2: Initial Dioxin (ppt) Correlation or Mean (n)	Model 2: p-Value: Unadjusted	Model 2: p-Value: Adjusted[a]
Current Alcohol Use (drinks/day)	n	869	1,251			482		
(continuous)		$\bar{x}$ = 0.68	$\bar{x}$ = 0.72	0.553	0.515	r=–0.058	0.207	0.793
(discrete)	0-1	684 (78.7)	1,015 (81.1)	0.040	0.037	$\bar{x}$ = 111.5 (n=385)	0.593	0.853
	>1-4	170 (19.6)	201 (16.1)			$\bar{x}$ = 100.4 (n=89)		
	>4	15 (1.7)	35 (2.8)			$\bar{x}$ = 98.8 (n=8)		
Lifetime Alcohol History (drink-years)	n	864	1,249			479		
(continuous)		$\bar{x}$ = 36.9	$\bar{x}$ = 37.0	0.970	0.918	r=0.074	0.104	0.041
(discrete)	0	54 (6.3)	64 (5.1)	0.393	0.349	$\bar{x}$ = 143.2 (n=34)	0.198	0.078
	>0-40	568 (65.7)	811 (64.9)			$\bar{x}$ = 106.8 (n=307)		
	>40	242 (28.0)	374 (29.9)			$\bar{x}$ = 106.8 (n=138)		

Table 8-2. Associations Between Alcohol Use and Estimates of Herbicide or Dioxin Exposure (Continued)

		Model 1				Model 2		
Covariate	Covariate Category	Ranch Hand Mean or n (%)	Comparison Mean or n (%)	p-Value: Unadjusted	p-Value: Adjusted[a]	Initial Dioxin (ppt) Correlation or Mean (n)	p-Value: Unadjusted	p-Value: Adjusted[a]
Current Wine Use (drinks/day)	n	869	1,251			482		
(continuous)		$\bar{x}$ = 0.15	$\bar{x}$ = 0.14	0.297	0.267	r=–0.095	0.038	0.701
(discrete)	0	503 (57.9)	717 (57.3)	0.829	0.793	$\bar{x}$ = 119.0 (n=316)	0.004	0.895
	>0	366 (42.1)	534 (42.7)			$\bar{x}$ = 92.6 (n=166)		
Lifetime Wine History (wine-years)	n	866	1,249			480		
(continuous)		$\bar{x}$ = 3.86	$\bar{x}$ = 3.03	0.028	0.022	r=–0.159	<0.001	0.121
(discrete)	0	261 (30.1)	332 (26.6)	0.082	0.056	$\bar{x}$ = 133.1 (n=166)	<0.001	0.265
	>0	605 (69.9)	917 (73.4)			$\bar{x}$ = 98.3 (n=314)		

Table 8-2. Associations Between Alcohol Use and Estimates of Herbicide or Dioxin Exposure (Continued)

		Model 3					
Covariate	Covariate Category	Comparison Mean or n (%)	Background Ranch Hand Mean or n (%)	Low Ranch Hand Mean or n (%)	High Ranch Hand Mean or n (%)	p-Value: Unadjusted	p-Value: Adjusted[a]
Current Alcohol Use (drinks/day)	n	1,213	380	239	243		
(continuous)		$\bar{x}$ = 0.72	$\bar{x}$ = 0.73	$\bar{x}$ = 0.66	$\bar{x}$ = 0.59	0.570	0.862
(discrete)	0-1	985 (81.2)	296 (77.9)	189 (79.1)	196 (80.7)	0.279	0.252
	>1-4	194 (16.0)	78 (20.5)	46 (19.3)	43 (17.7)		
	>4	34 (2.8)	6 (1.6)	4 (1.7)	4 (1.7)		
Lifetime Alcohol History (drink-years)	n	1,212	378	238	241		
(continuous)		$\bar{x}$ = 37.1	$\bar{x}$ = 34.7	$\bar{x}$ = 35.6	$\bar{x}$ = 40.3	0.602	0.808
(discrete)	0	62 (5.1)	20 (5.3)	13 (5.5)	21 (8.7)	0.338	0.458
	>0-40	786 (64.9)	258 (68.3)	155 (65.1)	152 (63.1)		
	>40	364 (30.0)	100 (26.5)	70 (29.4)	68 (28.2)		
Current Wine Use (drinks/day)	n	1,213	380	239	243		
(continuous)		$\bar{x}$ = 0.14	$\bar{x}$ = 0.21	$\bar{x}$ = 0.15	$\bar{x}$ = 0.07	<0.001	0.756
(discrete)	0	694 (57.2)	184 (48.4)	143 (59.8)	173 (71.2)	<0.001	0.803
	>0	519 (42.8)	196 (51.6)	96 (40.2)	70 (28.8)		

Table 8-2. Associations Between Alcohol Use and Estimates of Herbicide or Dioxin Exposure (Continued)

		Model 3					
Covariate	Covariate Category	Comparison Mean or n (%)	Background Ranch Hand Mean or n (%)	Low Ranch Hand Mean or n (%)	High Ranch Hand Mean or n (%)	p-Value: Unadjusted	p-Value: Adjusted[a]
Lifetime Wine History (wine-years)	n	1,212	379	238	242		
(continuous)		$\bar{x} = 3.07$	$\bar{x} = 4.80$	$\bar{x} = 4.55$	$\bar{x} = 1.73$	<0.001	0.076
(discrete)	0	320 (26.4)	93 (24.5)	76 (31.9)	90 (37.2)	<0.001	0.061
	>0	892 (73.6)	286 (75.5)	162 (68.1)	152 (62.8)		

Table 8-2. Associations Between Alcohol Use and Estimates of Herbicide or Dioxin Exposure (Continued)

		Model 4		
Covariate	Covariate Category	1987 Dioxin (ppt) Correlation or Mean (n)	p-Value: Unadjusted	p-Value: Adjusted[a]
Current Alcohol Use (drinks/day)	n	862		
(continuous)		r=–0.044	0.197	0.920
(discrete)	0-1	$\bar{x}$ = 14.3 (n=681)	0.497	0.932
	>1-4	$\bar{x}$ = 12.8 (n=167)		
	>4	$\bar{x}$ = 13.4 (n=14)		
Lifetime Alcohol History (drink-years)	n	857		
(continuous)		r=0.053	0.122	0.237
(discrete)	0	$\bar{x}$ = 17.8 (n=54)	0.223	0.353
	>0-40	$\bar{x}$ = 13.6 (n=565)		
	>40	$\bar{x}$ = 14.1 (n=238)		
Current Wine Use (drinks/day)	n	862		
(continuous)		r=–0.126	<0.001	0.741
(discrete)	0	$\bar{x}$ = 16.5 (n=500)	<0.001	0.631
	>0	$\bar{x}$ = 11.2 (n=362)		

Table 8-2. Associations Between Alcohol Use and Estimates of Herbicide or Dioxin Exposure (Continued)

		Model 4		
Covariate	Covariate Category	1987 Dioxin (ppt) Correlation or Mean (n)	p-Value: Unadjusted	p-Value: Adjusted[a]
Lifetime Wine History (wine-years)	n	859		
(continuous)		r=–0.118	<0.001	0.616
(discrete)	0	$\bar{x}$ = 17.6 (n=259)	<0.001	0.566
	>0	$\bar{x}$ = 12.6 (n=600)		

[a] Adjusted for occupation.

Note: Means for discrete covariates were transformed from the logarithmic (base 2) scale for initial dioxin in Model 2 and from the ($\log_2$ (X+1)) scale for 1987 dioxin in Model 4.

Table 8-3. Associations Between Cigarette Smoking and Estimates of Herbicide or Dioxin Exposure

		Model 1				Model 2		
Covariate	Covariate Category	Ranch Hand Mean or n (%)	Comparison Mean or n (%)	p-Value: Unadjusted	p-Value: Adjusted[a]	Initial Dioxin (ppt) Correlation or Mean (n)	p-Value: Unadjusted	p-Value: Adjusted[a]
Current Cigarette Smoking (cigarettes/day)	n	869	1,251			482		
(continuous)		$\bar{x}$ = 4.4	$\bar{x}$ = 4.0	0.311	0.325	r=0.045	0.328	0.450
(discrete)	0 (Never Smoked)	240 (27.6)	355 (28.4)	0.829	0.826	$\bar{x}$ = 110.9 (n=131)	0.775	0.388
	0 (Former Smoker)	453 (52.1)	663 (53.0)			$\bar{x}$ = 105.2 (n=252)		
	0-20	117 (13.5)	155 (12.4)			$\bar{x}$ = 117.8 (n=64)		
	>20	59 (6.8)	78 (6.2)			$\bar{x}$ = 117.2 (n=35)		
Lifetime Cigarette Smoking) (pack-years)	n	868	1,250			481		
(continuous)		$\bar{x}$ = 17.3	$\bar{x}$ = 16.5	0.434	0.519	r=–0.040	0.377	0.203
(discrete)	0	240 (27.7)	355 (28.4)	0.886	0.869	$\bar{x}$ = 110.9 (n=131)	0.498	0.203
	>0-10	233 (26.8)	325 (26.0)			$\bar{x}$ = 117.2 (n=129)		
	>10	395 (45.5)	570 (45.6)			$\bar{x}$ = 104.1 (n=221)		

Table 8-3. Associations Between Cigarette Smoking and Estimates of Herbicide or Dioxin Exposure (Continued)

		Model 3					
Covariate	Covariate Category	Comparison Mean or n (%)	Background Ranch Hand Mean or n (%)	Low Ranch Hand Mean or n (%)	High Ranch Hand Mean or n (%)	p-Value: Unadjusted	p-Value: Adjusted[a]
Current Cigarette Smoking (cigarettes/day)	n	1,213	380	239	243		
(continuous)		$\bar{x} = 3.98$	$\bar{x} = 4.43$	$\bar{x} = 4.04$	$\bar{x} = 4.96$	0.518	0.047
(discrete)	0 (Never Smoked)	344 (28.4)	106 (27.9)	65 (27.2)	66 (27.2)	0.835	0.090
	0 (Former Smoker)	644 (53.1)	198 (52.1)	131 (54.8)	121 (49.8)		
	0-20	152 (12.5)	52 (13.7)	25 (10.5)	39 (16.1)		
	>20	73 (6.0)	24 (6.3)	18 (7.5)	17 (7.0)		
Lifetime Cigarette Smoking (pack-years)	n	1,212	380	238	243		
(continuous)		$\bar{x} = 16.4$	$\bar{x} = 16.1$	$\bar{x} = 19.7$	$\bar{x} = 17.0$	0.172	0.156
(discrete)	0	344 (28.4)	106 (27.9)	65 (27.3)	66 (27.2)	0.767	0.067
	>0-10	315 (26.0)	102 (26.8)	56 (23.5)	73 (30.0)		
	>10	553 (45.6)	172 (45.3)	117 (49.2)	104 (42.8)		

Table 8-3. Associations Between Cigarette Smoking and Estimates of Herbicide or Dioxin Exposure (Continued)

Covariate	Covariate Category	Model 4: 1987 Dioxin (ppt) Correlation or Mean (n)	Model 4: p-Value: Unadjusted	Model 4: p-Value: Adjusted[a]
Current Cigarette Smoking (cigarettes/day)	n	862		
(continuous)		r=–0.014	0.679	<0.001
(discrete)	0 (Never Smoked)	$\bar{x}$ = 14.5 (n=237)	0.889	<0.001
	0 (Former Smoker)	$\bar{x}$ = 13.9 (n=450)		
	0-20	$\bar{x}$ = 13.2 (n=116)		
	>20	$\bar{x}$ = 14.2 (n=59)		
Lifetime Cigarette Smoking (pack-years)	n	861		
(continuous)		r=–0.006	0.861	0.039
(discrete)	0	$\bar{x}$ = 14.5 (n=237)	0.434	<0.001
	>0-10	$\bar{x}$ = 14.8 (n=231)		
	>10	$\bar{x}$ = 13.3 (n=393)		

[a] Adjusted for occupation.

Note: Means for discrete covariates were transformed from the logarithmic (base 2) scale for initial dioxin in Model 2 and from the ($\log_2$ (X+1)) scale for 1987 dioxin in Model 4.

dioxin (p=0.039 for lifetime cigarette smoking in its continuous form; p<0.001 for all other analyses). The mean 1987 dioxin for those participants with more than 10 pack-years was lower (13.3 ppt) than participants with no smoking history (14.5 ppt) or smokers with no more than 10 pack-years (14.8 ppt). The adjusted analysis of Model 3 showed marginally significant results for the discrete forms of current smoking habits (p=0.090) and lifetime smoking history (p=0.067).

8.5 EXPOSURE TO CARCINOGENS

Results of tests of association between reported exposure to ionizing radiation, industrial chemicals, herbicides, insecticides, and degreasing chemicals and the estimates of dioxin exposure are presented in Table 8-4. These variables were constructed based on responses given by participants and were intended to indicate only post-Southeast Asia (SEA) exposures to these suspected carcinogens.

The association between reported degreasing chemical exposure and dioxin was significant in the analysis of Models 2, 3, and 4 (p<0.001 for each model); however, after adjusting for military occupation, the association between reported degreasing chemical exposure and dioxin levels was not significant in any of those three models (p>0.27 for all analyses).

Significant associations between group or dioxin levels and reported exposure to herbicides were revealed in Models 1, 3, and 4 (p<0.001, p<0.001, p=0.013, respectively). These associations were significant after adjustment for military occupation (p<0.001 for all analyses). In Model 1, more Ranch Hands (96.9%) than Comparisons (40.9%) reported herbicide exposure. Model 3 analyses showed a similar relation between Ranch Hands and Comparisons. In Model 4, Ranch Hands who reported exposure to herbicides had a mean 1987 dioxin level of 14.2 ppt, as compared to a mean 1987 dioxin level of 8.2 ppt for Ranch Hands who did not report exposure to herbicides. In Model 2, unadjusted and adjusted analysis showed no significant association between reported herbicide exposure and initial dioxin levels (p>0.39 for both analyses).

The association between industrial chemical exposure and dioxin was significant in the analysis of Models 2, 3, and 4 (p=0.030 for Model 2 and p<0.001 for Models 3 and 4); however, after adjusting for military occupation, these associations were no longer significant (p>0.46 for all analyses). Participants who reported exposure to industrial chemicals had higher mean dioxin levels in Models 2 and 4 than those participants who did not report exposure. In Model 3, the percentage of Ranch Hands reporting exposure to industrial chemicals increased with increasing dioxin levels. For Ranch Hands in the background dioxin category, 52.5 percent of participants reported exposure to industrial chemicals. For Ranch Hands in the low dioxin category, 65.7 percent reported exposure to industrial chemicals. For Ranch Hands in the high dioxin category, 74.5 percent reported exposure to industrial chemicals.

Significant associations were observed between insecticide exposure and group in Model 1 (p<0.001, unadjusted and adjusted), as well as between insecticide exposure and categorized dioxin in Model 3 (p<0.001, unadjusted and adjusted). In Model 1, 80.5 percent of Ranch Hands and 63.9 percent of Comparisons were exposed to insecticides. In Model 3, the percentage of participants exposed to insecticides was 64.0 among Comparisons, 79.5 among Ranch Hands in the background dioxin category, 82.0 among Ranch Hands in the low dioxin category, and 80.3 among Ranch Hands in the high dioxin category.

Table 8-4. Associations Between Exposure to Carcinogens and Estimates of Herbicide or Dioxin Exposure

		Model 1				Model 2		
Covariate	Covariate Category	Ranch Hand Mean or n (%)	Comparison Mean or n (%)	p-Value: Unadjusted	p-Value: Adjusted[a]	Initial Dioxin (ppt) Correlation or Mean (n)	p-Value: Unadjusted	p-Value: Adjusted[a]
Degreasing Chemical Exposure	n	870	1,251			482		
	Yes	571 (65.6)	795 (63.6)	0.348	0.299	$\bar{x}$ = 120.3 (n=360)	<0.001	0.922
	No	299 (34.4)	456 (36.5)			$\bar{x}$ = 81.9 (n=122)		
Herbicide Exposure	n	870	1,251			482		
	Yes	843 (96.9)	511 (40.9)	<0.001	<0.001	$\bar{x}$ = 108.7 (n=474)	0.399	0.781
	No	27 (3.1)	740 (59.2)			$\bar{x}$ = 143.1 (n=8)		
Industrial Chemical Exposure	n	870	1,251			482		
	Yes	541 (62.2)	776 (62.0)	0.979	0.934	$\bar{x}$ = 115.8 (n=338)	0.030	0.605
	No	329 (37.8)	475 (38.0)			$\bar{x}$ = 95.0 (n=144)		
Insecticide Exposure	n	870	1,251			482		
	Yes	700 (80.5)	799 (63.9)	<0.001	<0.001	$\bar{x}$ = 106.6 (n=391)	0.231	0.162
	No	170 (19.5)	452 (36.1)			$\bar{x}$ = 121.0 (n=91)		

Table 8-4. Associations Between Exposure to Carcinogens and Estimates of Herbicide or Dioxin Exposure (Continued)

		Model 1				Model 2		
Covariate	Covariate Category	Ranch Hand Mean or n (%)	Comparison Mean or n (%)	p-Value: Unadjusted	p-Value: Adjusted[a]	Initial Dioxin (ppt) Correlation or Mean (n)	p-Value: Unadjusted	p-Value: Adjusted[a]
Ionizing Radiation Exposure	n	870	1,251			482		
	Yes	194 (22.3)	344 (27.5)	0.008	0.005	$\bar{x}$ = 96.5 (n=109)	0.108	0.280
	No	676 (77.7)	907 (72.5)			$\bar{x}$ = 113.2 (n=373)		

Table 8-4. Associations Between Exposure to Carcinogens and Estimates of Herbicide or Dioxin Exposure (Continued)

		Model 3					
Covariate	**Covariate Category**	**Comparison Mean or n (%)**	**Background Ranch Hand Mean or n (%)**	**Low Ranch Hand Mean or n (%)**	**High Ranch Hand Mean or n (%)**	**p-Value Unadjusted**	**p-Value: Adjusted[a]**
Degreasing Chemical Exposure	n	1,213	381	239	243		
	Yes	780 (64.3)	209 (54.9)	158 (66.1)	202 (83.1)	<0.001	0.310
	No	433 (35.7)	172 (45.1)	81 (33.9)	41 (16.9)		
Herbicide Exposure	n	1,213	381	239	243		
	Yes	500 (41.2)	363 (95.3)	236 (98.7)	238 (97.9)	<0.001	<0.001
	No	713 (58.8)	18 (4.7)	3 (1.3)	5 (2.1)		
Industrial Chemical Exposure	n	1,213	381	239	243		
	Yes	758 (62.5)	200 (52.5)	157 (65.7)	181 (74.5)	<0.001	0.465
	No	455 (37.5)	181 (47.5)	82 (34.3)	62 (25.5)		
Insecticide Exposure	n	1,213	381	239	243		
	Yes	776 (64.0)	303 (79.5)	196 (82.0)	195 (80.3)	<0.001	<0.001
	No	437 (36.0)	78 (20.5)	43 (18.0)	48 (19.8)		
Ionizing Radiation Exposure	n	1,213	381	239	243		
	Yes	334 (27.5)	82 (21.5)	63 (26.4)	46 (18.9)	0.010	0.013
	No	879 (72.5)	299 (78.5)	176 (73.6)	197 (81.1)		

Table 8-4. Associations Between Exposure to Carcinogens and Estimates of Herbicide or Dioxin Exposure (Continued)

		Model 4		
Covariate	**Covariate Category**	**1987 Dioxin (ppt) Correlation or Mean (n)**	**p-Value: Unadjusted**	**p-Value: Adjusted[a]**
Degreasing Chemical Exposure	n	863		
	Yes	$\bar{x}$ = 16.9 (n=569)	<0.001	0.279
	No	$\bar{x}$ = 9.6 (n=294)		
Herbicide Exposure	n	863		
	Yes	$\bar{x}$ = 14.2 (n=837)	0.013	<0.001
	No	$\bar{x}$ = 8.2 (n=26)		
Industrial Chemical Exposure	n	863		
	Yes	$\bar{x}$ = 16.3 (n=538)	<0.001	0.633
	No	$\bar{x}$ = 10.8 (n=325)		
Insecticide Exposure	n	863		
	Yes	$\bar{x}$ = 14.0 (n=694)	0.967	0.583
	No	$\bar{x}$ = 14.0 (n=169)		

Table 8-4. Associations Between Exposure to Carcinogens and Estimates of Herbicide or Dioxin Exposure (Continued)

		Model 4		
Covariate	**Covariate Category**	**1987 Dioxin (ppt) Correlation or Mean (n)**	**p-Value: Unadjusted**	**p-Value: Adjusted[a]**
Ionizing Radiation Exposure	n	863		
	Yes	$\bar{x}$ = 12.9 (n=191)	0.261	0.546
	No	$\bar{x}$ = 14.3 (n=672)		

[a] Adjusted for occupation.

Note: Means for discrete covariates were transformed from the logarithmic (base 2) scale for initial dioxin in Model 2 and from the ($\log_2$ (X+1)) scale for 1987 dioxin in Model 4.

The Models 1 and 3 analyses showed significant associations between group and exposure to ionizing radiation for unadjusted and adjusted analysis. A significant difference between the percentage of participants who have been exposed to ionizing radiation was seen between Ranch Hands (22.3%) and Comparisons (27.5%) in Model 1 ($p=0.008$, unadjusted; $p=0.005$, adjusted). In Model 3, a significant difference in the percentage of participants who were exposed to ionizing radiation was seen among Comparisons (27.5%), Ranch Hands in the background dioxin category (21.5%), Ranch Hands in the low dioxin category (26.4%), and Ranch Hands in the high dioxin category (18.9%) ($p=0.010$, unadjusted; $p=0.013$, adjusted, for military occupation). No significant associations were seen between mean initial or 1987 dioxin levels and ionizing radiation exposure in Models 2 and 4 in the adjusted or unadjusted models ($p>0.10$ for all analyses).

8.6 HEALTH VARIABLES

Results of tests of association between numerous measures related to a participant's health and the estimates of dioxin exposure are presented in Table 8-5. In Model 1 analyses, both unadjusted and adjusted for military occupation, all associations between health variables and group were nonsignificant ($p>0.22$ for all analyses).

Statistically significant associations were found between the continuous and discrete forms of the body fat measurement and dioxin for Model 3 ($p<0.001$) and Model 4 ($p<0.001$) for both unadjusted and adjusted analyses. In Model 3, the mean body fat was 22.9 percent for Comparisons, 21.2 percent for Ranch Hands in the background dioxin category, 23.8 percent for Ranch Hands in the low dioxin category, and 24.3 percent for Ranch Hands in the high dioxin category. The association between body fat and 1987 dioxin was positive. For the continuous form of the body fat measurement, the unadjusted Model 2 analysis showed no significant association with initial dioxin ($p=0.106$); however, the results adjusted for military occupation were statistically significant ($p=0.048$), with a positive association between body fat and initial dioxin.

The association between the continuous form of cholesterol and initial dioxin was significant for Model 2 in the unadjusted analysis ($p=0.005$) and in the analysis adjusted for military occupation ($p=0.042$). Cholesterol increased as initial dioxin increased. The association between cholesterol and dioxin levels was significant or marginally significant in both the continuous and discrete forms for Models 3 and 4. When the analysis was adjusted for military occupation, the association was no longer significant in Model 3 ($p=0.176$, continuous; $p=0.293$, discrete). The positive association between cholesterol and 1987 dioxin based on the adjusted Model 4 analysis was marginally significant for the continuous form of cholesterol ($p=0.099$) and nonsignificant for the discrete form of Model 4 ($p=0.446$).

High-density lipoprotein (HDL) cholesterol in its continuous form showed significant or marginally significant associations with dioxin in Model 2 ($p=0.065$), Model 3 ($p=0.002$), and Model 4 ($p<0.001$). When adjusting for military occupation, the association became nonsignificant in Model 2 ($p=0.274$) and Model 3 ($p=0.188$). The adjusted association remained significant in Model 4 ($p=0.013$), with HDL levels decreasing as the mean dioxin levels increased. Stratifying participants into less than or equal to 35 mg/dl HDL or greater than 35 mg/dl HDL revealed no significant associations with dioxin levels in Models 2 through 4 for the adjusted or unadjusted analyses ($p>0.18$ for all analyses).

Table 8-5. Associations Between Health Variables and Estimates of Herbicide or Dioxin Exposure

		Model 1				Model 2		
Covariate	Covariate Category	Ranch Hand Mean or n (%)	Comparison Mean or n (%)	p-Value: Unadjusted	p-Value: Adjusted[a]	Initial Dioxin (ppt) Correlation or Mean (n)	p-Value: Unadjusted	p-Value: Adjusted[a]
Body Fat (percent)	n	870	1,251			482		
(continuous)		$\bar{x}$ = 22.8	$\bar{x}$ = 23.0	0.544	0.580	r=0.074	0.106	0.048
(discrete)	Lean or Normal (≤25%)	626 (72.0)	875 (69.9)	0.341	0.338	$\bar{x}$ = 109.2 (n=314)	0.989	0.952
	Obese (>25%)	244 (28.0)	376 (30.1)			$\bar{x}$ = 109.1 (n=168)		
Cholesterol (mg/dl)	n	870	1,251			482		
(continuous)		$\bar{x}$ = 212.6	$\bar{x}$ = 213.2	0.745	0.705	r=0.129	0.005	0.042
(discrete)	0-200	336 (38.6)	467 (37.3)	0.753	0.714	$\bar{x}$ = 100.3 (n=175)	0.211	0.520
	>200-239	345 (39.7)	516 (41.3)			$\bar{x}$ = 110.5 (n=190)		
	>239	189 (21.7)	268 (21.4)			$\bar{x}$ = 121.4 (n=117)		
HDL (mg/dl)	n	869	1,250			481		
(continuous)		$\bar{x}$ = 46.6	$\bar{x}$ = 46.4	0.679	0.688	r=–0.084	0.065	0.274
(discrete)	0-35	164 (18.9)	210 (16.8)	0.241	0.221	$\bar{x}$ = 108.2 (n=100)	0.898	0.270
	>35	705 (81.1)	1,040 (83.2)			$\bar{x}$ = 109.7 (n=381)		

Table 8-5. Associations Between Health Variables and Estimates of Herbicide or Dioxin Exposure (Continued)

		Model 1				Model 2		
Covariate	Covariate Category	Ranch Hand Mean or n (%)	Comparison Mean or n (%)	p-Value: Unadjusted	p-Value: Adjusted[a]	Initial Dioxin (ppt) Correlation or Mean (n)	p-Value: Unadjusted	p-Value: Adjusted[a]
Cholesterol-HDL Ratio	n	869	1,250			481		
(continuous)		$\bar{x}$ = 4.85	$\bar{x}$ = 4.85	0.961	0.945	r=0.143	0.002	0.100
(discrete)	0-5	510 (58.7)	738 (59.0)	0.907	0.847	$\bar{x}$ = 95.5 (n=263)	<0.001	0.038
	>5	359 (41.3)	512 (41.0)			$\bar{x}$ = 128.8 (n=218)		
Physical Activity Index	n	864	1,243			480		
	Sedentary	475 (55.0)	646 (52.0)	0.256	0.265	$\bar{x}$ = 121.1 (n=268)	0.001	0.022
	Moderate	157 (18.2)	259 (20.8)			$\bar{x}$ = 115.3 (n=86)		
	Very Active	232 (26.9)	338 (27.2)			$\bar{x}$ = 84.5 (n=126)		
Diabetic Class[b]	n	861	1,233	0.997	0.999	477	0.135	0.004
	Normal	601 (69.8)	862 (69.9)			$\bar{x}$ = 106.5 (n=303)		
	Impaired	113 (13.1)	161 (13.1)			$\bar{x}$ = 98.4 (n=66)		
	Diabetic	147 (17.1)	210 (17.0)			$\bar{x}$ = 127.0 (n=108)		
Family History of Diabetes	n	863	1,239			478		
	Yes	221 (25.6)	338 (27.3)	0.422	0.387	$\bar{x}$ = 116.4 (n=133)	0.368	0.353
	No	642 (74.4)	901 (72.7)			$\bar{x}$ = 107.0 (n=345)		

Table 8-5. Associations Between Health Variables and Estimates of Herbicide or Dioxin Exposure (Continued)

Covariate	Covariate Category	Model 1: Ranch Hand Mean or n (%)	Model 1: Comparison Mean or n (%)	Model 1: p-Value: Unadjusted	Model 1: p-Value: Adjusted[a]	Model 2: Initial Dioxin (ppt) Correlation or Mean (n)	Model 2: p-Value: Unadjusted	Model 2: p-Value: Adjusted[a]
Family History of Heart Disease	n	860	1,245			477		
	Yes	526 (61.2)	756 (60.7)	0.875	0.812	$\bar{x}$ = 111.6 (n=292)	0.599	0.429
	No	334 (38.8)	489 (39.3)			$\bar{x}$ = 106.7 (n=185)		
Family History of Heart Disease Before Age 45	n	848	1,229			471		
	Yes	107 (12.6)	146 (11.9)	0.662	0.617	$\bar{x}$ = 124.2 (n=63)	0.266	0.876
	No	741 (87.4)	1,083 (88.1)			$\bar{x}$ = 108.2 (n=408)		
Currently Taking Blood Pressure Medication	n	870	1,251			482		
	Yes	265 (30.5)	364 (29.1)	0.530	0.544	$\bar{x}$ = 107.1 (n=161)	0.748	0.838
	No	605 (69.5)	887 (70.9)			$\bar{x}$ = 110.2 (n=321)		

Table 8-5. Associations Between Health Variables and Estimates of Herbicide or Dioxin Exposure (Continued)

		Model 3					
Covariate	Covariate Category	Comparison Mean or n (%)	Background Ranch Hand Mean or n (%)	Low Ranch Hand Mean or n (%)	High Ranch Hand Mean or n (%)	p-Value: Unadjusted	p-Value: Adjusted[a]
Body Fat (percent)	n	1,213	381	239	243		
(continuous)		$\bar{x} = 22.9$	$\bar{x} = 21.2$	$\bar{x} = 23.8$	$\bar{x} = 24.3$	<0.001	<0.001
(discrete)	Lean or Normal (≤25%)	852 (70.2)	308 (80.8)	154 (64.4)	160 (65.8)	<0.001	<0.001
	Obese (>25%)	361 (29.8)	73 (19.2)	85 (35.6)	83 (34.2)		
Cholesterol (mg/dl)	n	1,213	381	239	243		
(continuous)		$\bar{x} = 213.2$	$\bar{x} = 210.4$	$\bar{x} = 210.3$	$\bar{x} = 218.4$	0.045	0.176
(discrete)	0-200	451 (37.2)	159 (41.7)	94 (39.3)	81 (33.3)	0.097	0.293
	>200-239	502 (41.4)	151 (39.6)	97 (40.6)	93 (38.3)		
	>239	260 (21.4)	71 (18.6)	48 (20.1)	69 (28.4)		
HDL (mg/dl)	n	1,212	381	238	243		
(continuous)		$\bar{x} = 46.3$	$\bar{x} = 48.0$	$\bar{x} = 46.8$	$\bar{x} = 44.1$	0.002	0.188
(discrete)	0-35	207 (17.1)	62 (16.3)	49 (20.6)	51 (21.0)	0.262	0.585
	>35	1,005 (82.9)	319 (83.7)	189 (79.4)	192 (79.0)		
Cholesterol-HDL Ratio	n	1,212	381	238	243		
(continuous)		$\bar{x} = 4.86$	$\bar{x} = 4.68$	$\bar{x} = 4.77$	$\bar{x} = 5.18$	<0.001	0.103
(discrete)	0-5	713 (58.8)	244 (64.0)	152 (63.9)	111 (45.7)	<0.001	0.028
	>5	499 (41.2)	137 (36.0)	86 (36.1)	132 (54.3)		

Table 8-5. Associations Between Health Variables and Estimates of Herbicide or Dioxin Exposure (Continued)

		Model 3					
Covariate	Covariate Category	Comparison Mean or n (%)	Background Ranch Hand Mean or n (%)	Low Ranch Hand Mean or n (%)	High Ranch Hand Mean or n (%)	p-Value: Unadjusted	p-Value: Adjusted[a]
Physical Activity Index	n	1,205	377	238	242		
	Sedentary	623 (51.7)	200 (53.1)	121 (50.8)	147 (60.7)	0.075	0.309
	Moderate	255 (21.2)	71 (18.8)	41 (17.2)	45 (18.6)		
	Very Active	327 (27.1)	106 (28.1)	76 (31.9)	50 (20.7)		
Diabetic Class[b]	n	1,196	379	236	241		
	Normal	841 (70.3)	295 (77.8)	151 (64.0)	152 (63.1)	<0.001	<0.001
	Impaired	155 (13.0)	47 (12.4)	35 (14.8)	31 (12.9)		
	Diabetic	200 (16.7)	37 (9.8)	50 (21.2)	58 (24.1)		
Family History of Diabetes	n	1,201	378	236	242		
	Yes	321 (26.7)	87 (23.0)	58 (24.6)	75 (31.0)	0.149	0.761
	No	880 (73.3)	291 (77.0)	178 (75.4)	167 (69.0)		
Family History of Heart Disease	n	1,207	376	235	242		
	Yes	729 (60.4)	230 (61.2)	141 (60.0)	151 (62.4)	0.936	0.565
	No	478 (39.6)	146 (38.8)	94 (40.0)	91 (37.6)		
Family History of Heart Disease Before Age 45	n	1,192	370	230	241		
	Yes	137 (11.5)	44 (11.9)	24 (10.4)	39 (16.2)	0.186	0.444
	No	1,055 (88.5)	326 (88.1)	206 (89.6)	202 (83.8)		

Table 8-5. Associations Between Health Variables and Estimates of Herbicide or Dioxin Exposure (Continued)

		Model 3					
Covariate	Covariate Category	Comparison Mean or n (%)	Background Ranch Hand Mean or n (%)	Low Ranch Hand Mean or n (%)	High Ranch Hand Mean or n (%)	p-Value: Unadjusted	p-Value: Adjusted[a]
Currently Taking Blood Pressure Medication	n	1,213	381	239	243		
	Yes	353 (29.1)	99 (26.0)	77 (32.2)	84 (34.6)	0.102	0.070
	No	860 (70.9)	282 (74.0)	162 (67.8)	159 (65.4)		

Table 8-5. Associations Between Health Variables and Estimates of Herbicide or Dioxin Exposure (Continued)

Covariate	Covariate Category	Model 4		
		1987 Dioxin (ppt) Correlation or Mean (n)	p-Value: Unadjusted	p-Value: Adjusted[a]
Body Fat (percent)	n	863		
(continuous)		r=0.257	<0.001	<0.001
(discrete)	Lean or Normal (≤25%)	$\bar{x}$ = 12.6 (n=622)	<0.001	<0.001
	Obese (>25%)	$\bar{x}$ = 18.4 (n=241)		
Cholesterol (mg/dl)	n	863		
(continuous)		r=0.097	0.004	0.099
(discrete)	0-200	$\bar{x}$ = 12.7 (n=334)	0.040	0.446
	>200-239	$\bar{x}$ = 14.1 (n=341)		
	>239	$\bar{x}$ = 16.4 (n=188)		
HDL (mg/dl)	n	862		
(continuous)		r=–0.131	<0.001	0.013
(discrete)	0-35	$\bar{x}$ = 15.5 (n=162)	0.188	0.621
	>35	$\bar{x}$ = 13.7 (n=700)		
Cholesterol-HDL Ratio	n	862		
(continuous)		r=0.152	<0.001	0.021
(discrete)	0-5	$\bar{x}$ = 12.2 (n=507)	<0.001	0.010
	>5	$\bar{x}$ = 16.9 (n=355)		

Table 8-5. Associations Between Health Variables and Estimates of Herbicide or Dioxin Exposure (Continued)

		Model 4		
Covariate	Covariate Category	1987 Dioxin (ppt) Correlation or Mean (n)	p-Value: Unadjusted	p-Value: Adjusted[a]
Physical Activity Index	n	857		
	Sedentary	$\bar{x}$ = 15.1 (n=468)	0.026	0.408
	Moderate	$\bar{x}$ = 14.5 (n=157)		
	Very Active	$\bar{x}$ = 11.9 (n=232)		
Diabetic Class[b]	n	856	<0.001	<0.001
	Normal	$\bar{x}$ = 12.7 (n=598)		
	Impaired	$\bar{x}$ = 13.9 (n=113)		
	Diabetic	$\bar{x}$ = 21.2 (n=145)		
Family History of Diabetes	n	856	0.065	0.198
	Yes	$\bar{x}$ = 15.8 (n=220)		
	No	$\bar{x}$ = 13.5 (n=636)		
Family History of Heart Disease	n	853		
	Yes	$\bar{x}$ = 14.3 (n=522)	0.580	0.177
	No	$\bar{x}$ = 13.7 (n=331)		

Table 8-5. Associations Between Health Variables and Estimates of Herbicide or Dioxin Exposure (Continued)

Covariate	Covariate Category	Model 4: 1987 Dioxin (ppt) Correlation or Mean (n)	Model 4: p-Value: Unadjusted	Model 4: p-Value: Adjusted[a]
Family History of Heart Disease Before Age 45	n	841		
	Yes	$\bar{x}$ = 16.3 (n=107)	0.148	0.979
	No	$\bar{x}$ = 13.8 (n=734)		
Currently Taking Blood Pressure Medication	n	863		
	Yes	$\bar{x}$ = 15.6 (n=260)	0.057	0.013
	No	$\bar{x}$ = 13.3 (n=603)		

[a] Adjusted for occupation.

[b] Diabetic Class: Normal: <140 mg/dl 2-hour postprandial glucose
Impaired: ≥140-<200 mg/dl 2-hour postprandial glucose
Diabetic: Verified past history of diabetes or ≥200 mg/dl 2-hour postprandial glucose.

Note: Means for discrete covariates were transformed from the logarithmic (base 2) scale for initial dioxin in Model 2 and from the ($\log_2$ (X+1)) scale for 1987 dioxin in Model 4.

Statistically significant unadjusted associations were found between the cholesterol-HDL ratio and dioxin for Model 2 (p=0.002), Model 3 (p<0.001), and Model 4 (p<0.001). In Models 2 and 3, the association was not significant when adjusting for military occupation (p=0.100 for Model 2; p=0.103 for Model 3). In Model 4, the association between 1987 dioxin and the cholesterol-HDL ratio remained significant after adjusting for military occupation (p=0.021). As 1987 dioxin levels increased, the cholesterol-HDL ratio increased.

Dichotomizing the cholesterol-HDL ratio using a cutpoint of 5.0 revealed significant associations with dioxin for Models 2, 3, and 4 (p<0.001 for these models). The associations between the categorized cholesterol-HDL ratio and dioxin levels remained significant after adjusted for military occupation (p<0.04 for all analyses). The mean dioxin levels were greater for participants with a higher cholesterol-HDL ratio in Models 2 and 4. In Model 3, a significant difference between the percentage of participants with a ratio less than 5.0 was seen among Comparisons (58.8%), Ranch Hands in the background dioxin category (64.0%), Ranch Hands in the low dioxin category (63.9%), and Ranch Hands in the high dioxin category (45.7%).

The examination of the physical activity index showed a significant association with dioxin in Model 2 (p=0.001) and Model 4 (p=0.026), and a marginally significant relation in Model 3 (p=0.075) in the unadjusted analysis. In Models 2 and 4, the mean dioxin levels were decreased as activity levels increased. When adjusting for military occupation, the associations seen in Models 3 and 4 were no longer significant (p=0.309 for Model 3; p=0.408 for Model 4). Model 2 analysis showed a significant association between physical activity and initial dioxin levels after adjusting for military occupation (p=0.022).

A significant association between diabetic class and dioxin was revealed in Models 3 and 4 (p<0.001 for both models), and the results remained significant (p<0.001) after adjusting for military occupation. In Model 3, a significant difference between the percentage of participants classified as normal, impaired, and diabetic was seen among Comparisons, Ranch Hands in the background dioxin category, Ranch Hands in the low dioxin category, and Ranch Hands in the high dioxin category. More participants were classified as diabetic as the dioxin levels increased. For Ranch Hands in the background dioxin category, 9.8 percent of participants were classified as diabetic. For Ranch Hands in the low dioxin category, 21.2 percent were classified as diabetic, and 24.1 percent of Ranch Hands in the high dioxin category were classified as diabetic. In Model 4, participants classified as diabetic had higher mean 1987 dioxin levels than participants classified as impaired or normal. Model 2 showed a significant association between diabetic class and initial dioxin levels only when adjusting for military occupation (p=0.004).

The analysis of family history of diabetes revealed no significant associations with dioxin levels in Models 1, 2, and 3 in the unadjusted or adjusted analyses. Model 4 showed a marginally significant association in the unadjusted model only (p=0.065).

No significant associations were observed between family history of heart disease or family history of heart disease before age 45 and any of the estimates of herbicide or dioxin exposure (p>0.14 for all analyses).

When examining the relation between current blood pressure medication use and dioxin exposure, no significant relation was observed in Model 2, whether or not adjustment was made for military occupation (p>0.74 for both analyses). In Model 3, the unadjusted analysis showed no significant association (p=0.102), but the adjusted showed a marginally significant association (p=0.070). In Model 4, the unadjusted analysis was marginally significant (p=0.057), and the adjusted analysis showed a

significant association ($p=0.013$). Mean 1987 dioxin levels were higher in those participants currently taking medication for high blood pressure (15.6 ppt) than for those not taking the medication (13.3 ppt).

8.7 SUN EXPOSURE VARIABLES

Results of tests of association between a participant's reaction to sun exposure and the estimates of dioxin exposure are shown in Table 8-6. These statistics are based on non-Black participants, because the sun exposure covariates were used in adjusted analyses of skin neoplasms only, and Blacks were excluded from the skin neoplasm analyses.

Unadjusted analysis of the relation between skin color and dioxin exposure showed no significant associations ($p \geq 0.12$ for all unadjusted analyses). When the associations were tested adjusting for military occupation, Models 3 and 4 showed a significant association ($p=0.050$ for Model 3; $p=0.006$ for Model 4). The highest percentage of participants with peach skin color was for Ranch Hands in the low dioxin category (82.4%). Participants with peach skin color had a higher mean 1987 dioxin level than participants with non-peach skin color (14.5 ppt vs. 12.5 ppt; $p=0.006$, adjusted for military occupation).

A significant association between hair color and dioxin levels was observed in Model 2 ($p<0.001$) and Model 3 ($p=0.006$), and a marginally significant association was seen in Model 4 ($p=0.055$). The association was no longer significant when adjusting for military occupation in Model 2 ($p=0.155$) or Model 4 ($p=0.715$), but remained significant in Model 3 ($p=0.048$). The percentage of participants with black or dark brown hair varied among the Comparisons (69.0%), Ranch Hands in the background dioxin category (66.9%), Ranch Hands in the low dioxin category (59.7%), and Ranch Hands in the high dioxin category (74.8%).

Significant associations were observed between eye color and dioxin exposure in the unadjusted analysis of all four models ($p<0.04$ for all unadjusted analyses). These results remained significant ($p<0.04$) after adjusting for military occupation in all models except Model 3, which still showed a marginally significant association ($p=0.088$). In Model 2 and Model 4, participants with brown eyes had higher initial and 1987 dioxin levels than participants with other eye colors.

Unadjusted analysis of average lifetime residential latitude revealed significant associations with dioxin exposure in Model 1 ($p=0.004$), Model 2 ($p=0.032$), and Model 3 ($p=0.011$). In Model 1, a significant difference between the percentage of participants living, on average, closer to the equator (less than 37 degrees latitude) was seen between Ranch Hands (46.5%) and Comparisons (53.2%). In Model 2, the mean initial dioxin levels were greater for participants living closer to the equator. In Model 3, a significant difference between the percentage of participants living, on average, closer to the equator was seen among Comparisons (52.9%), Ranch Hands in the background dioxin category (46.4%), Ranch Hands in the low dioxin category (42.1%), and Ranch Hands in the high dioxin category (50.0%). Analyses of the relation between group or dioxin and average lifetime residential latitude also was significant after adjustment for the effects of military occupation in Models 1, 2, and 3 ($p=0.002$, $p=0.028$, and $p=0.007$, respectively). While no significant association was seen in the unadjusted analysis of Model 4 ($p=0.152$), the association between latitude was significant when adjusting for military occupation ($p=0.021$).

Table 8-6. Associations Between Sun Exposure Variables and Estimates of Herbicide or Dioxin Exposure (Non-Blacks Only)

Covariate	Covariate Category	Model 1: Ranch Hand Mean or n (%)	Model 1: Comparison Mean or n (%)	Model 1: p-Value: Unadjusted	Model 1: p-Value: Adjusted[a]	Model 2: Initial Dioxin (ppt) Correlation or Mean (n)	Model 2: p-Value: Unadjusted	Model 2: p-Value: Adjusted[a]
Skin Color	n	815	1,178			446		
	Peach	637 (78.2)	897 (76.2)	0.319	0.308	$\bar{x}$ = 111.3 (n=360)	0.884	0.789
	Non-Peach	178 (21.8)	281 (23.9)			$\bar{x}$ = 113.2 (n=86)		
Hair Color	n	815	1,176			446		
	Black, Dark Brown	549 (67.4)	810 (68.9)	0.506	0.497	$\bar{x}$ = 123.7 (n=301)	<0.001	0.155
	Light Brown, Blonde, Red, Bald	266 (32.6)	366 (31.1)			$\bar{x}$ = 90.4 (n=145)		
Eye Color	n	815	1,178			446		
	Brown	229 (28.1)	383 (32.5)	0.016	0.015	$\bar{x}$ = 135.3 (n=132)	0.014	0.023
	Hazel, Green	242 (29.7)	287 (24.4)			$\bar{x}$ = 98.7 (n=133)		
	Gray, Blue	344 (42.2)	508 (43.1)			$\bar{x}$ = 106.3 (n=181)		

Table 8-6. Associations Between Sun Exposure Variables and Estimates of Herbicide or Dioxin Exposure (Non-Blacks Only) (Continued)

		Model 1				Model 2		
Covariate	Covariate Category	Ranch Hand Mean or n (%)	Comparison Mean or n (%)	p-Value: Unadjusted	p-Value: Adjusted[a]	Initial Dioxin (ppt) Correlation or Mean (n)	p-Value: Unadjusted	p-Value: Adjusted[a]
Reaction of Skin to Sun After at Least 2 Hours	n	814	1,178			446		
	No Reaction	294 (36.1)	427 (36.3)	0.859	0.855	$\bar{x}$ = 122.5 (n=169)	0.221	0.243
	Becomes Red	322 (39.6)	481 (40.8)			$\bar{x}$ = 109.7 (n=176)		
	Burns	127 (15.6)	178 (15.1)			$\bar{x}$ = 93.0 (n=68)		
	Painfully Burns	71 (8.7)	92 (7.8)			$\bar{x}$ = 111.8 (n=33)		
Reaction of Skin to Sun After Repeated Exposure	n	814	1,178			446		
	Tans Dark Brown	225 (27.6)	331 (28.1)	0.978	0.976	$\bar{x}$ = 116.6 (n=131)	0.417	0.485
	Tans Moderately	409 (50.3)	580 (49.2)			$\bar{x}$ = 109.0 (n=218)		
	Tans Mildly	151 (18.6)	224 (19.0)			$\bar{x}$ = 119.6 (n=78)		
	Freckles with No Tan	29 (3.6)	43 (3.7)			$\bar{x}$ = 82.7 (n=19)		

Table 8-6. Associations Between Sun Exposure Variables and Estimates of Herbicide or Dioxin Exposure (Non-Blacks Only) (Continued)

		Model 1				Model 2		
Covariate	Covariate Category	Ranch Hand Mean or n (%)	Comparison Mean or n (%)	p-Value: Unadjusted	p-Value: Adjusted[a]	Initial Dioxin (ppt) Correlation or Mean (n)	p-Value: Unadjusted	p-Value: Adjusted[a]
Composite Sun-Reaction Index	n	814	1,178			446		
	High	91 (11.2)	110 (9.3)	0.330	0.333	$\bar{x}$ = 103.6 (n=45)	0.820	0.871
	Medium	187 (23.0)	291 (24.7)			$\bar{x}$ = 110.3 (n=102)		
	Low	536 (65.9)	777 (66.0)			$\bar{x}$ = 113.4 (n=299)		
Average Lifetime Residential Latitude	n	815	1,178			446		
	<37°	379 (46.5)	627 (53.2)	0.004	0.002	$\bar{x}$ = 123.6 (n=206)	0.032	0.028
	≥37°	436 (53.5)	551 (46.8)			$\bar{x}$ = 102.4 (n=240)		

Table 8-6. *Associations Between Sun Exposure Variables and Estimates of Herbicide or Dioxin Exposure (Non-Blacks Only) (Continued)*

Covariate	Covariate Category	Model 3: Comparison Mean or n (%)	Model 3: Background Ranch Hand Mean or n (%)	Model 3: Low Ranch Hand Mean or n (%)	Model 3: High Ranch Hand Mean or n (%)	p-Value: Unadjusted	p-Value: Adjusted[a]
Skin Color	n	1,143	362	216	230		
	Peach	873 (76.4)	273 (75.4)	178 (82.4)	182 (79.1)	0.179	0.050
	Non-Peach	270 (23.6)	89 (24.6)	38 (17.6)	48 (20.9)		
Hair Color	n	1,141	362	216	230		
	Black, Dark Brown	787 (69.0)	242 (66.9)	129 (59.7)	172 (74.8)	0.006	0.048
	Light Brown, Blonde, Red, Bald	354 (31.0)	120 (33.1)	87 (40.3)	58 (25.2)		
Eye Color	n	1,143	362	216	230		
	Brown	366 (32.0)	95 (26.2)	53 (24.5)	79 (34.4)	0.039	0.088
	Hazel, Green	283 (24.8)	106 (29.3)	70 (32.4)	63 (27.4)		
	Gray, Blue	494 (43.2)	161 (44.5)	93 (43.1)	88 (38.3)		
Reaction of Skin to Sun After at Least 2 Hours	n	1,143	361	216	230		
	No Reaction	410 (35.9)	122 (33.8)	74 (34.3)	95 (41.3)	0.644	0.994
	Becomes Red	471 (41.2)	144 (39.9)	89 (41.2)	87 (37.8)		
	Burns	174 (15.2)	57 (15.8)	35 (16.2)	33 (14.4)		
	Painfully Burns	88 (7.7)	38 (10.5)	18 (8.3)	15 (6.5)		

Table 8-6. Associations Between Sun Exposure Variables and Estimates of Herbicide or Dioxin Exposure (Non-Blacks Only) (Continued)

		Model 3					
Covariate	Covariate Category	Comparison Mean or n (%)	Background Ranch Hand Mean or n (%)	Low Ranch Hand Mean or n (%)	High Ranch Hand Mean or n (%)	p-Value: Unadjusted	p-Value: Adjusted[a]
Reaction of Skin to Sun After Repeated Exposure	n	1,143	361	216	230		
	Tans Dark Brown	315 (27.6)	90 (24.9)	60 (27.8)	71 (30.9)	0.533	0.768
	Tans Moderately	571 (50.0)	188 (52.1)	106 (49.1)	112 (48.7)		
	Tans Mildly	217 (19.0)	73 (20.2)	37 (17.1)	41 (17.8)		
	Freckles with No Tan	40 (3.5)	10 (2.8)	13 (6.0)	6 (2.6)		
Composite Sun-Reaction Index	n	1,143	361	216	230		
	High	105 (9.2)	46 (12.7)	25 (11.6)	20 (8.7)	0.480	0.815
	Medium	285 (24.9)	83 (23.0)	48 (22.2)	54 (23.5)		
	Low	753 (65.9)	232 (64.3)	143 (66.2)	156 (67.8)		
Average Lifetime Residential Latitude	n	1,143	362	216	230		
	<37°	605 (52.9)	168 (46.4)	91 (42.1)	115 (50.0)	0.011	0.007
	≥37°	538 (47.1)	194 (53.6)	125 (57.9)	115 (50.0)		

Table 8-6. Associations Between Sun Exposure Variables and Estimates of Herbicide or Dioxin Exposure (Non-Blacks Only) (Continued)

		Model 4		
Covariate	Covariate Category	1987 Dioxin (ppt) Correlation or Mean (n)	p-Value: Unadjusted	p-Value: Adjusted[a]
Skin Color	n	808		
	Peach	$\bar{x}$ = 14.5 (n=633)	0.120	0.006
	Non-Peach	$\bar{x}$ = 12.5 (n=175)		
Hair Color	n	808		
	Black, Dark Brown	$\bar{x}$ = 14.8 (n=543)	0.055	0.715
	Light Brown, Blonde, Red, Bald	$\bar{x}$ = 12.6 (n=265)		
Eye Color	n	808		
	Brown	$\bar{x}$ = 16.8 (n=227)	0.015	0.037
	Hazel, Green	$\bar{x}$ = 13.1 (n=239)		
	Gray, Blue	$\bar{x}$ = 13.1 (n=342)		
Reaction of Skin to Sun After at Least 2 Hours	n	807		
	No Reaction	$\bar{x}$ = 15.3 (n=291)	0.229	0.694
	Becomes Red	$\bar{x}$ = 14.1 (n=320)		
	Burns	$\bar{x}$ = 12.7 (n=125)		
	Painfully Burns	$\bar{x}$ = 12.0 (n=71)		

Table 8-6. Associations Between Sun Exposure Variables and Estimates of Herbicide or Dioxin Exposure (Non-Blacks Only) (Continued)

Covariate	Covariate Category	Model 4: 1987 Dioxin (ppt) Correlation or Mean (n)	Model 4: p-Value: Unadjusted	Model 4: p-Value: Adjusted[a]
Reaction of Skin to Sun After Repeated Exposure	n	807		
	Tans Dark Brown	$\bar{x}$ = 15.6 (n=221)	0.463	0.822
	Tans Moderately	$\bar{x}$ = 13.5 (n=406)		
	Tans Mildly	$\bar{x}$ = 13.7 (n=151)		
	Freckles with No Tan	$\bar{x}$ = 14.2 (n=29)		
Composite Sun-Reaction Index	n	807		
	High	$\bar{x}$ = 12.2 (n=91)	0.419	0.837
	Medium	$\bar{x}$ = 14.1 (n=185)		
	Low	$\bar{x}$ = 14.4 (n=531)		
Average Lifetime Residential Latitude	n	808		
	<37°	$\bar{x}$ = 14.9 (n=374)	0.152	0.021
	≥37°	$\bar{x}$ = 13.4 (n=434)		

[a] Adjusted for occupation.

Note: Means for discrete covariates were transformed from the logarithmic (base 2) scale for initial dioxin in Model 2 and from the ($\log_2$ (X+1)) scale for 1987 dioxin in Model 4.

No significant associations were observed between group or dioxin levels and reaction of skin to sun after at least 2 hours, reaction of skin to sun after repeated exposures, or a composite sun-reaction index for either the adjusted or unadjusted analyses ($p>0.22$ for all analyses).

8.8 OTHER MISCELLANEOUS COVARIATES

Results of tests of association between other miscellaneous covariates and the estimates of dioxin exposure are shown in Table 8-7. Examining the association between current total household income in both its continuous and discrete forms and dioxin revealed significant relations in the analysis of Models 2 through 4. By adjusting for military occupation, the association between income and dioxin levels was not significant ($p>0.08$) for continuous or discrete forms of income or for any of the models.

No significant associations were seen between group or dioxin levels and personality type, either unadjusted or adjusted for military occupation ($p>0.14$ for all analyses).

The relation between education and group was nonsignificant ($p=0.339$, unadjusted; $p=0.270$, adjusted, for military occupation). A significant relation between education and dioxin was revealed for Models 2 through 4 ($p\leq0.001$ for each model); however, after adjusting for military occupation, no significant relations were observed in Models 2, 3, or 4 ($p>0.20$ for all analyses).

The relation between current employment status and dioxin exposure mirrored the relation between education and dioxin exposure. Significant relations were seen in Models 2, 3, and 4 in the unadjusted analysis, but the relations were no longer significant when adjusted for military occupation ($p>0.39$ for all analyses).

In the analysis of current marital status and dioxin exposure, a marginally significant association was seen in Model 2 ($p=0.082$), and a significant relation was seen in Model 3 ($p=0.033$). After adjusting for military occupation, however, these associations were no longer significant ($p=0.282$ for Model 2; $p=0.635$ for Model 3).

Current parental status (having a child younger than 18 years old) was shown to have a marginally significant relation with dioxin in Model 2 ($p=0.066$) and Model 3 ($p=0.069$), and a significant relation with dioxin in Model 4 ($p=0.014$). Similar to current marital status, these relations were no longer significant when adjusting for military occupation ($p=0.979$, $p=0.644$, and $p=0.961$ for Models 2, 3, and 4, respectively).

The analysis of participants who reported having worked with vibrating power equipment or tools for 30 days or more revealed a significant association with initial dioxin ($p=0.033$) in Model 2 and with 1987 dioxin ($p=0.013$) in Model 4. Participants who worked with vibrating power equipment or tools had greater average initial and 1987 dioxin levels than participants who did not report having worked with vibrating power equipment or tools. After adjustment for military occupation, these associations became nonsignificant ($p=0.537$ for Model 2; $p=0.394$ for Model 4). All tests of association in Models 1 and 3 were nonsignificant for this covariate ($p>0.14$ for each analysis).

Tests of the association between reported exposure to heavy metals (worked for 30 days or more with lead, mercury, chromium, nickel, copper, cadmium, manganese, arsenic, selenium, or molybdenum) and

Table 8-7. Associations Between Other Miscellaneous Covariates and Estimates of Herbicide or Dioxin Exposure

		Model 1				Model 2		
Covariate	Covariate Category	Ranch Hand Mean or n (%)	Comparison Mean or n (%)	p-Value: Unadjusted	p-Value: Adjusted[a]	Initial Dioxin (ppt) Correlation or Mean (n)	p-Value: Unadjusted	p-Value: Adjusted[a]
Current Total Household Income (dollars)	n	861	1,236			478		
(continuous)		$\bar{x}$ = \$66,013	$\bar{x}$ = \$65,546	0.697	0.666	r=–0.187	<0.001	0.367
(discrete)	≤ \$65,000	438 (50.9)	628 (50.8)	0.999	0.956	$\bar{x}$ = 121.3 (n=267)	0.003	0.771
	> \$65,000	423 (49.1)	608 (49.2)			$\bar{x}$ = 94.7 (n=211)		
Personality Type	n	867	1,251			481		
	Type A	351 (40.5)	469 (37.5)	0.178	0.148	$\bar{x}$ = 106.0 (n=184)	0.590	0.740
	Type B	516 (59.5)	782 (62.5)			$\bar{x}$ = 111.1 (n=297)		
Education	n	869	1,251			482		
	High School	456 (52.5)	684 (54.7)	0.339	0.270	$\bar{x}$ = 93.1 (n=201)	0.001	0.261
	College	413 (47.5)	567 (45.3)			$\bar{x}$ = 122.3 (n=281)		
Current Employment Status	n	869	1,251			482		
	Yes	564 (64.9)	825 (66.0)	0.652	0.719	$\bar{x}$ = 116.6 (n=319)	0.027	0.836
	No	305 (35.1)	426 (34.1)			$\bar{x}$ = 96.0 (n=163)		

Table 8-7. *Associations Between Other Miscellaneous Covariates and Estimates of Herbicide or Dioxin Exposure (Continued)*

		Model 1				Model 2		
Covariate	Covariate Category	Ranch Hand Mean or n (%)	Comparison Mean or n (%)	p-Value: Unadjusted	p-Value: Adjusted[a]	Initial Dioxin (ppt) Correlation or Mean (n)	p-Value: Unadjusted	p-Value: Adjusted[a]
Current Marital Status	n	869	1,251			482		
	Married	714 (82.2)	1,031 (82.4)	0.928	0.823	$\bar{x}$ = 105.3 (n=386)	0.082	0.282
	Not Married	155 (17.8)	220 (17.6)			$\bar{x}$ = 126.2 (n=96)		
Current Parental Status (Child Younger than 18 Years of Age)	n	869	1,251			482		
	Yes	110 (12.7)	181 (14.5)	0.260	0.301	$\bar{x}$ = 132.1 (n=67)	0.066	0.979
	No	759 (87.3)	1,070 (85.5)			$\bar{x}$ = 105.9 (n=415)		
Worked with Vibrating Power Equipment or Tools	n	869	1,249			482		
	Yes	246 (28.3)	328 (26.3)	0.321	0.287	$\bar{x}$ = 124.5 (n=150)	0.033	0.537
	No	623 (71.7)	921 (73.7)			$\bar{x}$ = 102.9 (n=332)		
Composite Exposure to Heavy Metals	n	869	1,251			482		
	Yes	110 (12.7)	178 (14.2)	0.330	0.288	$\bar{x}$ = 116.0 (n=77)	0.522	0.401
	No	759 (87.3)	1,073 (85.8)			$\bar{x}$ = 107.9 (n=405)		

Table 8-7. Associations Between Other Miscellaneous Covariates and Estimates of Herbicide or Dioxin Exposure (Continued)

		Model 3					
Covariate	Covariate Category	Comparison Mean or n (%)	Background Ranch Hand Mean or n (%)	Low Ranch Hand Mean or n (%)	High Ranch Hand Mean or n (%)	p-Value: Unadjusted	p-Value: Adjusted[a]
Current Total Household Income (dollars)	n	1,199	376	237	241		
(continuous)		$\bar{x}$ = $65,894	$\bar{x}$ = $70,625	$\bar{x}$ = $66,698	$\bar{x}$ = $58,081	<0.001	0.835
(discrete)	≤ $65,000	603 (50.3)	167 (44.4)	114 (48.1)	153 (63.5)	<0.001	0.692
	> $65,000	596 (49.7)	209 (55.6)	123 (51.9)	88 (36.5)		
Personality Type	n	1,213	379	239	242		
	Type A	457 (37.7)	164 (43.3)	87 (36.4)	97 (40.1)	0.205	0.264
	Type B	756 (62.3)	215 (56.7)	152 (63.6)	145 (59.9)		
Education	n	1,213	380	239	243		
	High School	549 (45.3)	130 (34.2)	119 (49.8)	162 (66.7)	<0.001	0.357
	College	664 (54.7)	250 (65.8)	120 (50.2)	81 (33.3)		
Current Employment Status	n	1,213	380	239	243		
	Yes	806 (66.5)	240 (63.2)	144 (60.3)	175 (72.0)	0.031	0.398
	No	407 (33.6)	140 (36.8)	95 (39.8)	68 (28.0)		
Current Marital Status	n	1,213	380	239	243		
	Married	1,006 (82.9)	322 (84.7)	201 (84.1)	185 (76.1)	0.033	0.635
	Not Married	207 (7.1)	58 (15.3)	38 (15.9)	58 (23.9)		

Table 8-7. Associations Between Other Miscellaneous Covariates and Estimates of Herbicide or Dioxin Exposure (Continued)

		Model 3					
Covariate	Covariate Category	Comparison Mean or n (%)	Background Ranch Hand Mean or n (%)	Low Ranch Hand Mean or n (%)	High Ranch Hand Mean or n (%)	p-Value: Unadjusted	p-Value: Adjusted[a]
Current Parental Status (Child Younger than 18 Years of Age)	n	1,213	380	239	243		
	Yes	176 (14.5)	41 (10.8)	26 (10.9)	41 (16.9)	0.069	0.644
	No	1,037 (85.5)	339 (89.2)	213 (89.1)	202 (83.1)		
Worked with Vibrating Power Equipment or Tools	n	1,211	380	239	243		
	Yes	318 (26.3)	95 (25.0)	72 (30.1)	78 (32.1)	0.142	0.242
	No	893 (73.7)	285 (75.0)	167 (69.9)	165 (67.9)		
Composite Exposure to Heavy Metals	n	1,213	380	239	243		
	Yes	174 (14.3)	33 (8.7)	35 (14.6)	42 (17.3)	0.010	0.347
	No	1,039 (85.7)	347 (91.3)	204 (85.4)	201 (82.7)		

Table 8-7. Associations Between Other Miscellaneous Covariates and Estimates of Herbicide or Dioxin Exposure (Continued)

Covariate	Covariate Category	Model 4 1987 Dioxin (ppt) Correlation or Mean (n)	p-Value: Unadjusted	p-Value: Adjusted[a]
Current Total Household Income (dollars)	n	854		
(continuous)		r=–0.169	<0.001	0.185
(discrete)	≤ $65,000	$\bar{x}$ = 15.9 (n=434)	<0.001	0.083
	> $65,000	$\bar{x}$ = 12.3 (n=420)		
Personality Type	n	860		
	Type A	$\bar{x}$ = 13.4 (n=348)	0.314	0.671
	Type B	$\bar{x}$ = 14.5 (n=512)		
Education	n	862		
	High School	$\bar{x}$ = 18.2 (n=411)	<0.001	0.203
	College	$\bar{x}$ = 11.0 (n=451)		
Current Employment Status	n	862		
	Yes	$\bar{x}$ = 15.0 (n=559)	0.013	0.878
	No	$\bar{x}$ = 12.4 (n=303)		
Current Marital Status	n	862		
	Married	$\bar{x}$ = 13.6 (n=708)	0.119	0.794
	Not Married	$\bar{x}$ = 15.9 (n=154)		

Table 8-7. Associations Between Other Miscellaneous Covariates and Estimates of Herbicide or Dioxin Exposure (Continued)

		Model 4		
Covariate	Covariate Category	1987 Dioxin (ppt) Correlation or Mean (n)	p-Value: Unadjusted	p-Value: Adjusted[a]
Current Parental Status (Child Younger than 18 Years of Age)	n	862		
	Yes	$\bar{x}$ = 17.8 (n=108)	0.014	0.961
	No	$\bar{x}$ = 13.5 (n=754)		
Worked with Vibrating Power Equipment or Tools	n	862		
	Yes	$\bar{x}$ = 16.2 (n=245)	0.013	0.394
	No	$\bar{x}$ = 13.2 (n=617)		
Composite Exposure to Heavy Metals	n	862		
	Yes	$\bar{x}$ = 18.1 (n=110)	0.007	0.854
	No	$\bar{x}$ = 13.5 (n=752)		

[a] Adjusted for occupation.

Note: Means for discrete covariates were transformed from the logarithmic (base 2) scale for initial dioxin in Model 2 and from the ($\log_2$ (X+1)) scale for 1987 dioxin in Model 4.

dioxin were significant for categorized dioxin in Model 3 (p=0.010) and 1987 dioxin in Model 4 (p=0.007). The percentage of Ranch Hands exposed to heavy metals increased as dioxin increased in Model 3 analyses (8.7% for Ranch Hands in the background dioxin category, 14.6% for Ranch Hands in the low dioxin category, and 17.3% for Ranch Hands in the high dioxin category). After adjustment for occupation, the association was nonsignificant (p=0.347). In Model 4, average 1987 dioxin levels were greater for participants reporting exposure to heavy metals than for participants not reporting exposure to heavy metals. The association between exposure to heavy metals and 1987 dioxin was nonsignificant after adjustment for military occupation (p=0.854). All tests of association between reported exposure to heavy metals and group in Model 1 were nonsignificant (p>0.28 for both analyses). Tests of association between reported exposure to heavy metals and initial dioxin in Model 2 also were nonsignificant (p>0.40 for both analyses).

8.9 SUMMARY

The purpose of this chapter was to determine whether the covariates used throughout this report were associated with the estimates of herbicide or dioxin exposure. Military occupation, being associated with education, may have influenced the associations between covariates and dioxin estimates. Therefore, associations between covariates and the estimates of exposure in this chapter were adjusted for military occupation but not for other known or suspected confounders. Associations between covariates and dioxin estimates should be interpreted with caution and do not necessarily reflect a causal relation.

The demographic variables of age, race, and military occupation were used as matching variables in the original study design. As expected because of the matching, there were no significant differences between Ranch Hands and Comparisons for these three variables. As exhibited in previous reports, dioxin was significantly associated with military occupation. Officers had the lowest levels, followed by enlisted flyers and enlisted groundcrew. Because the Ranch Hand enlisted groundcrew tended to be younger on average than the Ranch Hand officers and enlisted flyers, a strong negative association also was seen between dioxin levels and age. When military occupation was taken into consideration, however, dioxin exposure estimates did not appear to be related to age. Race exhibited significant associations with dioxin in that Black participants appeared to have lower dioxin levels than non-Black participants. The effect of race on dioxin levels was strengthened when military occupation was considered.

Few significant associations were seen between current alcohol use or lifetime alcohol history and group or dioxin. Wine use appeared to affect dioxin exposure estimates significantly. Lower dioxin levels were associated with more wine use, both current and lifetime. As suspected in previous reports, this phenomenon appears to be related to military occupation as officers may have consumed more wine than did enlisted personnel. When adjusting for military occupation, the association between wine use and dioxin exposure was not significant.

Significant associations were observed between current cigarette smoking and lifetime cigarette smoking history and 1987 dioxin after adjustment for military occupation.

Questions posed to the participants regarding exposure to known carcinogens were intended to indicate post-SEA exposures; however, the data suggest that the participants may have included SEA exposures as well. Significant associations were seen between dioxin and both degreasing chemicals and industrial chemicals. Adjusted analysis showed that these associations were related to military occupation. It is believed that fewer officers were exposed to industrial chemicals and degreasing chemicals than enlisted personnel. The percentage of Comparisons exposed to ionizing radiation was larger than the percentage

of Ranch Hands exposed; however, a greater percentage of Ranch Hands was exposed to herbicides and insecticides and may indicate that Ranch Hands were more likely to report SEA or pre-SEA exposures as well.

The significant associations between dioxin and health measurements, such as cholesterol, HDL, the cholesterol-HDL ratio, physical activity level, and diabetic class, are likely to be explained by body fat. Higher body fat measurements are known to correspond to higher dioxin levels, lower levels of HDL cholesterol, and higher cholesterol-HDL ratios, as well as diabetes. Also, higher body fat is more likely to occur with sedentary lifestyles.

Of covariates related to sun exposure, Ranch Hands with darker hair tended to have higher levels of initial dioxin than those with lighter-colored hair. The relation between dioxin and hair color was explained by military occupation. Dioxin estimates appeared to differ with eye color in that those with brown eyes tended to have higher dioxin levels. Although eye and hair color are related, from the adjusted analysis, it did not appear that the relation between eye color and dioxin could be explained by military occupation. A larger percentage of Ranch Hands lived in latitudes farther from the equator than did Comparisons, and higher levels of dioxin were seen for those participants who live in more southerly latitudes. No significant associations were observed with the reaction to sun exposure covariates.

The relations between dioxin and current total household income, education, current employment status, current marital status, and having a child younger than 18 years old appear to be directly related to military occupation. Participants who were officers at the time of service in SEA have larger current incomes than participants who were enlisted at the time of service in SEA. Officers have the lowest dioxin levels (Table 2-8); consequently, there was a negative association between income and dioxin. A larger percentage of Ranch Hand officers tended to be college graduates than enlisted personnel, and, consequently, college graduates had lower dioxin levels than high school graduates. Differences in current employment may be due to age, income, and level of education. Current marital and parental status may be related to military occupation directly or indirectly through the relation between military occupation and socioeconomic factors.

8.10 CONCLUSION

The purpose of this chapter was to determine whether the covariates used throughout this report were associated with the estimates of dioxin exposure and, therefore, could potentially be confounding variables in subsequent statistical analyses in this report. Military occupation, being associated with education, may have influenced the associations between covariates and dioxin estimates. The associations between covariates and the estimates of dioxin exposure in this chapter were adjusted for military occupation, but not for other known or suspected confounders. Therefore, associations between covariates and dioxin estimates should be interpreted with caution.

In general, the Ranch Hand and Comparison groups were similar for the majority of the covariates; however, exceptions included reported herbicide exposure, insecticide exposure, and average lifetime latitude. A greater percentage of Ranch Hands than Comparisons reported herbicide exposure. Although the questionnaire had been structured to indicate post-SEA exposure only, a possible explanation for this association between group and herbicide exposure may have been the tendency of Ranch Hands to report their exposure to dioxin during their time of duty in SEA. A greater percentage of Ranch Hands reported exposure to insecticides than did Comparisons. More Comparisons than Ranch Hands lived in the more southerly latitudes. Ranch Hands who lived in the more southerly latitudes had a higher average initial and 1987 dioxin level than Ranch Hands living in the more northerly latitudes.

Most of the significant associations between dioxin and the covariates in the Ranch Hand group can be explained at least partially by the effects of military occupation or body fat. Of the three occupational cohorts, enlisted groundcrew had the highest levels of 1987 and initial dioxin. Adjusted analyses in the clinical chapters fully account for group, age, occupation, and other potential confounders to further investigate significant associations between covariates and dioxin. Body fat and the half-life of dioxin were known to be related, and the Models 2 and 3 analyses in the clinical chapters adjusted for body fat. In addition, body fat was used as a risk factor where appropriate. The reader is referred to these chapters for a more complete assessment of the effect of dioxin on the relevant medical endpoints.

Table of Contents

List of Tables

9 GENERAL HEALTH ASSESSMENT

9.1 INTRODUCTION

9.1.1 Background

In February 1991, in response to unanswered questions and ongoing concerns that Vietnam veterans may have been harmed by herbicide defoliants, Congress passed the Agent Orange Act of 1991. Under this legislation, Public Law 102-4, the National Academy of Sciences requested the Institute of Medicine (IOM) to conduct an independent review of all the scientific evidence relevant to the issue and to make recommendations for the directions of future research. The committee established by the IOM expanded its review beyond studies of veterans to include reports in the world literature of other populations exposed to dioxin by occupation, environmental contamination, or as a consequence of industrial accidents. The first IOM report (1), *Veterans and Agent Orange*, was published in 1994, and the first biennial update was published in 1996 (2). These references provide an inclusive resource of information on the health consequences of exposure to herbicides and, particularly, to dioxin. Among the valuable contributions was the stratification of suspect diseases into three categories—"Sufficient," "Limited/Suggestive," and "Inadequate/Insufficient"—based on the scientific evidence for and against an association with herbicide exposure.

Pertinent to the Air Force Health Study (AFHS), the IOM Committee concluded that the principal limitation of most epidemiological studies was the lack of accurate and quantitative indices of individual exposure and that studies such as the AFHS, which include tissue levels in the analyses, have limitations. Despite these concerns and caveats, the committee emphasized the merits of the model of the AFHS and proposed that a similar methodology be applied to a study of the only other veteran group with significant herbicide exposure—the Army Chemical Corps. In its first recommendation, the committee endorsed the continued follow-up of the Air Force Ranch Hand and Comparison cohorts, now in its fifteenth year.

Although the potentially lethal consequences of acute phenoxy herbicide toxication have been well defined (3, 4), the latent effects of herbicide exposure on human health remain controversial. Epidemiological studies published in the scientific literature have focused on specific clinical endpoints, particularly malignancy, and have been based on cohorts of Vietnam veterans (5-15), on civilian populations exposed to dioxins by occupation (16-28), or as a consequence of industrial accidents (29–37). These studies and others have been summarized in the comprehensive literature reviews cited above (1, 2) and those of the Veterans Health Services and Research Administration published since the last AFHS examination (38–40).

The scientific basis for these epidemiological studies in humans has been firmly established in animal studies conducted over several decades. In laboratory animals, dioxin toxicity is species- and strain-specific and appears to correlate with the presence of a stereospecific protein receptor, the aryl hydrocarbon (Ah) receptor, found in the cytosol of selected organs and capable of binding aromatic hydrocarbons (41–44). The assessment of the risk of dioxin exposure to human health is in large part based on the molecular and cellular mechanisms of dioxin toxicity in animals and has been the subject of numerous review articles (45–50). Ah receptors have been isolated in the tissue of several human organs (43, 51–54), and the comparative properties of animal and human Ah receptors have been studied (55,

56). Epidemiological studies have focused on target organ effects that have been defined in animal models including immunotoxicity, carcinogenicity, hepatotoxicity, and neurotoxicity. In the chapters that follow, these and other clinical endpoints will be considered in detail.

The lack of an accurate measure of exposure is now recognized as the principal methodological limitation common to all of the early epidemiological investigations into the effects of herbicides on human health. Assay techniques developed a decade ago (57) now permit the accurate detection and quantitative measurement of trace amounts of dioxin in blood and adipose tissue and the identification of those with significant prior exposure to dioxin. Analyses of serum dioxin data from the AFHS (58) and two other epidemiological studies (59, 60) have been published and have contributed to a better understanding of the pharmacokinetics of dioxin in man. The reliability and reproducibility of the serum dioxin assay have been established (61) and the potential effects of age, body fat, and time since exposure on the rate of dioxin elimination have been explored (58). Based on the analyses of serial serum dioxin levels taken from participants in the current study 15 to 25 years after exposure, the latest estimate of the half-life of dioxin in humans has been revised upward to 8.7 years (58). These recent analyses have confirmed an earlier report (62) that an increase in body fat is associated with prolongation of the dioxin half-life, a finding that may be relevant to the development of clinical endpoints related to obesity.

The serum dioxin assay is important to the credibility of this and other epidemiological studies. The Centers for Disease Control and Prevention study of serum dioxin levels demonstrated that all estimates of herbicide exposure employed previously in Vietnam veterans were imprecise and that there was no significant difference in the current body burden of dioxin between most Vietnam and non-Vietnam veterans of the same era (63, 64). Published reports leave no doubt that, of all veterans who served in Vietnam, the 1,300 Air Force Ranch Hand personnel were among those most highly exposed to dioxin and that, within this group, the enlisted groundcrew responsible for handling the herbicides and for maintaining the spray equipment were at greatest exposure risk (8, 9, 65).

The importance of the serum dioxin assay is reflected in the number of publications reporting serum dioxin levels in exposed populations around the world including the United States (16, 65–70), Germany (71–73), Russia (74, 75), New Zealand (76), Austria (77), Australia (78), and Italy (35, 79). Apart from the current study, only a few published reports have appeared relating clinical and laboratory indices to serum or adipose dioxin levels (16, 36, 37, 80-83). Because these studies relate health outcomes with evidence of prior exposure to dioxin, they will receive special attention in the chapters that follow.

In this and previous AFHS examinations, five variables have been included in the general health assessment: self-perception of health, appearance of illness or distress during the examination, relative age, body fat, and erythrocyte sedimentation rate. In the Serum Dioxin Analysis Report of the 1987 examination (8), positive associations were noted between measured levels of dioxin and the perception of ill health and body fat. In the 1992 examinations, these associations were again found to be significant (9).

Finally, with the exception of the 1992 examinations, a significantly higher prevalence of elevated erythrocyte sedimentation rates was noted in the Ranch Hands relative to the Comparison cohort. In a more recent study (80), one of the few to correlate laboratory indices with the current body burden of dioxin, a positive association was found between the serum dioxin level and the erythrocyte sedimentation rate. These results have raised the possibility of a subclinical dioxin-induced inflammatory process and point to the need for continued surveillance in this and the final AFHS examination in 2002.

9.1.2 Summary of Previous Analyses of the Air Force Health Study

9.1.2.1 1982 Baseline Study Summary Results

Five general health variables were included in the 1982 baseline examination: self-perception of health, appearance of illness or distress, relative age, body fat, and erythrocyte sedimentation rate. In the analysis of the baseline examination data, a statistically significant difference in self-perception of health was found between the Ranch Hand and Comparison groups, with a greater percentage of Ranch Hands reporting their health as fair or poor than Comparisons (20.6% vs. 14.2%). This was true in both the younger and older age groups (Est. RR=1.82, p=0.017 for individuals 40 or younger and Est. RR=1.35, p=0.025 for individuals older than 40). Because only 9 of 1,811 individuals were reported by the examining physician as appearing ill or distressed, this designation was apparently reserved for only very ill or distressed individuals. Nevertheless, eight of the nine individuals were Ranch Hands, the difference being of marginal significance (p=0.056). Conversely, more Ranch Hands than Comparisons were reported by the examiners as appearing younger than their actual ages (4.9% vs. 2.5%, p=0.029). No overall differences in body fat or erythrocyte sedimentation rate were found, although a significant interaction between group and age for erythrocyte sedimentation rate was noted; younger Ranch Hands had fewer erythrocyte sedimentation rate abnormalities than did Comparisons, whereas no difference was found in participants older than 40.

9.1.2.2 1985 Follow-up Study Summary Results

General physical health was evaluated by the same five measures used in the baseline examination (self-perception of health, appearance of illness or distress, relative age, body fat, and erythrocyte sedimentation rate). The Ranch Hands again rated their health as fair or poor more often than the Comparisons (9.1% vs. 7.3%, respectively), although this difference was not statistically significant. Further analysis revealed a significant group-by-occupation interaction. Differences were largely confined to the enlisted groundcrew category where the adjusted relative risk was 1.90 (p=0.003).

Ten individuals were reported as appearing acutely ill or distressed at the 1985 follow-up examination. In contrast to the baseline examination, four were Ranch Hands and six were Comparisons; thus, no group difference was suggested. Relative age, as determined by the examining physician, was not significantly different in the two groups.

The (geometric) mean erythrocyte sedimentation rates did not differ significantly, either unadjusted or after adjustment for age, race, occupation, personality score, and an age-by-personality score interaction. In the discrete analysis, 5.8 percent of the Ranch Hands had erythrocyte sedimentation rate abnormalities (>20 mm/hr), contrasted to 3.6 percent in the Comparison group. This difference was significant both unadjusted (p=0.013) and adjusted for age and personality score (p=0.011).

The mean body fat of the Ranch Hands was significantly lower than the Comparisons (21.10 percent vs. 21.54 percent, p=0.037), and the difference was of nearly the same magnitude after adjustment for age, race, and occupation.

Longitudinal differences between the 1982 baseline and the 1985 follow-up examination were assessed by analyses of two discrete variables: self-perception of health and erythrocyte sedimentation rate. Analysis of self-perception of health showed no significant group differences in the change over time, with the Ranch Hand and Comparison groups reporting symmetrical improvements in their perceptions over the 3-year period. The erythrocyte sedimentation rate analysis revealed a highly significant group difference (p=0.002), because of a reversal of findings between examinations (i.e., a significant adverse

effect in the [younger] Comparisons at the baseline examination versus a significant adverse effect in the Ranch Hands at the follow-up examination).

9.1.2.3 1987 Follow-up Study Summary Results

The general health in the Ranch Hand and Comparison groups was assessed by the same five measures used in previous AFHS examinations: self-perception of health, appearance of illness or distress, relative age, body fat, and erythrocyte sedimentation rate. There were no significant group differences, either unadjusted or adjusted for covariates (age, race, occupation, and, in the case of self-perception of health and erythrocyte sedimentation rate, personality type), nor were there any significant group-by-covariate interactions for self-perception of health, appearance of illness or distress, relative age, or percent body fat. There was little difference in the geometric mean values of erythrocyte sedimentation rate in the two groups, but Ranch Hands had a significantly higher percentage of individuals with an abnormal erythrocyte sedimentation rate (>20 mm/hr) than Comparisons. For erythrocyte sedimentation rate, there was a significant difference between groups in the change from baseline to the 1987 follow-up examination, with a relatively greater number of Ranch Hands than Comparisons shifting from normal at baseline to abnormal at the follow-up examination. Only three participants (two Ranch Hands and one Comparison) were found to have rates in excess of 100 mm/hr; one of these (a Comparison) proved to have lung cancer and died in early 1989. No diagnosis was established for either of the two Ranch Hands during the course of the 1987 examination. Longitudinal analyses revealed a similar decline in both groups over time in the percentage of individuals reporting their health as fair or poor.

9.1.2.4 Serum Dioxin Analysis of 1987 Follow-up Study Summary Results

In general, body fat and erythrocyte sedimentation rate exhibited significant positive associations with initial dioxin. The other variables exhibited positive but nonsignificant associations with initial dioxin. The unadjusted and adjusted analyses of relative age appearance exhibited significant interactions between current dioxin and time since tour of duty. For Ranch Hands with 18.6 years or less since the end of duty in Southeast Asia (SEA), the associations between relative age and current dioxin were positive and at least marginally significant for each analysis type and assumption. For the other variables, the current dioxin-by-time analyses generally displayed nonsignificant but positive associations with current dioxin.

In general, the unadjusted and adjusted analyses for the four current dioxin categories overall exhibited significant contrasts for body fat and erythrocyte sedimentation rate, and the high versus background contrast and the low versus background contrast were significant with the Ranch Hands exceeding Comparisons. The body fat results for the four current dioxin categories displayed an increasing association with dioxin within the Ranch Hands (i.e., unknown, low, and high categories); however, the background category for Comparisons exceeded the unknown category for Ranch Hands.

The longitudinal analyses of self-perception of health demonstrated significant positive associations with initial dioxin and current dioxin. The percentage of participants who reported fair or poor health decreased by more than 50 percent from 1982 to 1987. In the longitudinal analyses of erythrocyte sedimentation rate, the percentages of abnormalities in 1987 differed significantly among the current dioxin categories.

In summary, with the exception of the erythrocyte sedimentation rate, the data analyzed in the general health assessment did not reveal any adverse health effect consequent to herbicide exposure or to the current body burden of dioxin.

9.1.2.5 1992 Follow-up Study Summary Results

In the assessment of general health, significant differences between Ranch Hands and Comparisons—the enlisted groundcrew in particular—were evident for self-perception of health. Significant associations between negative self-perception of health and initial and current levels of dioxin also were evident. These results are consistent with the 1985 and 1987 follow-up examinations. In contrast to self-perception of health, no significant results were found for the appearance of illness or distress and relative age appearance, which were recorded by the examining physicians.

The analyses of body fat displayed a significant positive association with current dioxin, whether calculated on a whole-weight or lipid-adjusted basis. Erythrocyte sedimentation rate also displayed a significant positive association with current dioxin levels.

In the longitudinal analysis, the increase in the percentage of Ranch Hands who perceived their health to be poor in 1992 from those that were normal in 1982 was significantly associated with initial dioxin levels. Relative age appearance also displayed a significant positive association with initial dioxin. The change in body fat from 1982 to 1992 was significantly associated with initial dioxin, and a significant difference between Ranch Hands and Comparisons also was found, especially in enlisted groundcrew.

9.1.3 Parameters for the 1997 General Health Assessment

9.1.3.1 Dependent Variables

The general health assessment was based on data from the 1997 questionnaire, physical examination, and laboratory data.

9.1.3.1.1 Questionnaire Data

During the health interview given to each participant, the following question was asked: "Compared to other people your age, would you say your health is excellent, good, fair, or poor?" This self-reported perception was analyzed as a measure of the general health status of each participant, although it was recognized that the perception was susceptible to varying degrees of conscious and subconscious bias (most participants were aware of their serum dioxin levels). This variable was dichotomized as "excellent or good" and "fair or poor" for statistical analyses. No participants were excluded for medical reasons from the analysis of this variable.

9.1.3.1.2 Physical Examination Data

Three variables derived from the 1997 Scripps Clinic physical examination were analyzed in the assessment of general health. For the first variable, the physician at the examination recorded the appearance of illness or distress (yes, no) of the study participant. For the second variable, the physician noted the appearance of the subject as younger than, older than, or the same as his stated age. This variable was dichotomized as "older than" and "same as or younger than" for statistical analyses. To the degree that the examining physicians were kept blind to the participant's group membership, these assessments were less subject to bias than the self-perception of health.

The third variable, body fat, was a measure of the relative body mass of an individual and was calculated from height (in meters) and weight (in kilograms) recorded at the physical examination. Non-ambulatory participants were weighed on a Scale-Tronix® 6006, which allowed a participant to be weighed in a wheelchair, if necessary. Body fat was calculated from a metric body mass index (84); the formula is

$$Body\ Fat\,(in\ percent) = \frac{Weight\,(kg)}{[Height\,(m)\,]^2} \bullet 1.264 - 13.305.$$

This variable was analyzed in both the discrete and continuous forms. For purposes of discrete analyses, body fat was dichotomized as "lean or normal" (≤25 percent) and "obese" (>25 percent). Lean participants (less than 10 percent body fat) were categorized with normal participants because few of the people in this study fit this definition (nine participants: six Comparisons and three Ranch Hands). This variable did not reflect changes in weight since time of duty in SEA. No participants were excluded for medical reasons from the analyses of these three variables.

9.1.3.1.3 Laboratory Examination Data

The erythrocyte sedimentation rate (mm/hr), measured at the laboratory examination, was analyzed. Although nonspecific, a high erythrocyte sedimentation rate generally indicates an ongoing disease process. This variable was analyzed in both the discrete and continuous forms. No participants were excluded for medical reasons from the analysis of this variable.

9.1.3.2 Covariates

The effects of the covariates age, race (Black, non-Black), military occupation (officer, enlisted flyer, enlisted groundcrew), current cigarette smoking, lifetime cigarette smoking history, current alcohol use, and lifetime alcohol history were used for analyses with all dependent variables.

Age, race, and military occupation were determined from military records. Lifetime alcohol history was based on information from the 1997 questionnaire and combined with similar information gathered at the 1987 and 1992 follow-up examinations. Each participant was asked about his drinking patterns throughout his lifetime. When a participant's drinking pattern changed, he was asked to describe how his alcohol consumption differed and the duration of time that the drinking pattern lasted. The participant's average daily alcohol consumption was determined for each of the reported drinking pattern periods throughout his lifetime, and an estimate of the corresponding total number of drink-years was derived. One drink-year was the equivalent of drinking 1.5 ounces of an 80-proof alcoholic beverage, one 12-ounce beer, or one 5-ounce glass of wine per day for 1 year. Current alcohol use was defined as the average number of drinks per day during the month prior to completing the questionnaire.

Current cigarette smoking and lifetime cigarette smoking history were based on questionnaire data. For lifetime cigarette smoking history, the respondent's average smoking was estimated over his lifetime based on his responses to the 1997 questionnaire, with 1 pack-year defined as 365 packs of cigarettes smoked during a single year.

Personality type (Type A, Type B) was used as a covariate in the analysis of self-perception of health and sedimentation rate only. Personality type was determined from the Jenkins Activity Survey administered during the 1997 follow-up examination and was derived from a discriminant-function equation based on questions that best discriminate men judged to be Type A from those judged to be Type B (85). Positive scores reflect the Type A direction; negative scores reflect the Type B direction. Personality type was dichotomized as Type A or Type B for all analyses of self-perception of health and erythrocyte sedimentation rate.

9.1.4 Statistical Methods

Table 9-1 summarizes the statistical analyses performed for the general health assessment. The first part of this table describes the dependent variables and identifies the covariates, exclusions, and the statistical methods. The second part of the table further describes the covariates. A covariate was used in its continuous form whenever possible for all adjusted analyses. If the covariate was inherently discrete (e.g., military occupation), or if a categorized form was needed to develop measures of association with the dependent variables, the covariate was categorized as shown in Table 9-1.

Cutpoints for erythrocyte sedimentation rate were age-dependent. Consequently, normal and abnormal levels for erythrocyte sedimentation rate were constructed according to a participant's laboratory value and age at the physical examination. The age-specific cutpoints also are listed in Table 9-1, and the reference ages for these cutpoints are given in parentheses following the cutpoints.

Table 9-2 provides a summary of the number of participants with missing dependent variable and covariate data.

Table 9-1. Statistical Analysis for the General Health Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions	Statistical Analysis and Methods
Self-perception of Health	Q-SR	D	Fair or Poor Excellent or Good	(1)	None	U:LR A:LR L:LR
Appearance of Illness Or Distress as Assessed by Physician	PE	D	Yes No	(2)	None	U:LR A:LR L:LR,CS
Relative Age Appearance as Assessed by Physician	PE	D	Older Same or Younger	(2)	None	U:LR A:LR L:LR
Body Fat (percent)	PE	D/C	Obese: >25% Lean or Normal: ≤25%	(2)	None	U:LR,GLM A:LR,GLM L:LR,GLM
Erythrocyte Sedimentation Rate (mm/hr)	LAB	D/C	Abnormal: >15 (Age 40–49) >20 (Age ≥50) Normal: ≤15 (Age 40–49) ≤20 (Age ≥50)	(1)	None	U:LR,GLM A:LR,GLM L:LR,GLM

[a] Covariates:
(1): age, race, military occupation, current cigarette smoking, lifetime cigarette smoking history, current alcohol use, lifetime alcohol history, personality type.
(2): age, race, military occupation, current cigarette smoking, lifetime cigarette smoking history, current alcohol use, lifetime alcohol history.

Table 9-1. Statistical Analysis for the General Health Assessment (Continued)

Covariates

Variable (Units)	Data Source	Data Form	Cutpoints
Age (years)	MIL	D/C	Born ≥ 1942 Born < 1942
Race	MIL	D	Black Non-Black
Occupation	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Current Cigarette Smoking (cigarettes/day)	Q-SR	D/C	0-Never 0-Former >0–20 >20
Lifetime Cigarette Smoking History (pack-years)	Q-SR	D/C	0 >0–10 >10
Current Alcohol Use (drinks/day)	Q-SR	D/C	0–1 >1–4 >4
Lifetime Alcohol History (drink-years)	Q-SR	D/C	0 >0–40 >40
Personality Type	PE	D	A Direction B Direction

Abbreviations

Data Source: LAB: 1997 laboratory results
MIL: Air Force military records
PE: 1997 physical examination
Q-SR: 1997 health questionnaire (self-reported)

Data Form: D: Discrete analysis only
D/C: Discrete and continuous analyses for dependent variables; appropriate form for analysis (either discrete or continuous) for covariates

Statistical Analysis: U: Unadjusted analysis
A: Adjusted analysis
L: Longitudinal analysis

Statistical Methods: CS: Chi-square contingency table analysis (continuity-adjusted)
GLM: General linear models analysis
LR: Logistic regression analysis
TT: Two-sample t-test

Table 9-2. Number of Participants with Missing Data for the General Health Assessment

Variable	Variable Use	Group: Ranch Hand	Group: Comparison	Dioxin (Ranch Hands Only): Initial	Dioxin (Ranch Hands Only): 1987	Categorized Dioxin: Ranch Hand	Categorized Dioxin: Comparison
Self-perception of Health	DEP	1	0	0	1	1	0
Erythrocyte Sedimentation Rate	DEP	0	1	0	0	0	0
Personality Type	COV	3	0	1	3	3	0
Current Cigarette Smoking	COV	1	0	0	1	1	0
Lifetime Cigarette Smoking History	COV	2	1	1	2	2	1
Current Alcohol Use	COV	1	0	0	1	1	0
Lifetime Alcohol History	COV	6	2	3	6	6	1

Note: DEP = Dependent variable.
COV = Covariate.
870 Ranch Hands and 1,251 Comparisons.
482 Ranch Hands for initial dioxin; 863 Ranch Hands for 1987 dioxin.
863 Ranch Hands and 1,213 Comparisons for categorized dioxin.

9.1.4.1 *Longitudinal Analysis*

Longitudinal analyses on all of the variables described above (self-perception of health, appearance of illness or distress by the physician, relative age, body fat, and erythrocyte sedimentation rate) were conducted to evaluate the changes between the 1982 baseline examination and the 1997 follow-up examination.

The erythrocyte sedimentation rate abnormal cutpoints differ by examination date and age. For the 1982 baseline examination, the cutpoint was 12 mm/hr for all participants (that is, erythrocyte sedimentation rates greater than 12 mm/hr were considered abnormal). For the 1985, 1987, 1992, and 1997 follow-up examinations, the cutpoint was 15 mm/hr for participants younger than 50 and 20 mm/hr for participants at least 50 years old at the time of the examination. A participant was considered to be normal or abnormal based on his age and the cutpoint at the given examination for discrete analyses. Methods of compensation for the change in cutpoints over time for the continuous analyses include the use of age and the measurement in 1982 as covariates.

9.2 RESULTS

9.2.1 Dependent Variable-Covariate Associations

The results of covariate associations with each dependent variable are documented in Appendix F, Table F-1. These associations are pairwise between the dependent variable and the covariate and are not adjusted for any other covariates. These results are discussed below.

Tests of associations for self-perception of health revealed significant associations with race, occupation, current cigarette smoking, and lifetime cigarette smoking history (p=0.010, p=0.001, p=0.001, and p=0.001, respectively). The percentage of Blacks who perceived their health to be fair or poor was 19.5 percent, compared to 11.5 percent for non-Blacks. Enlisted groundcrew reported their health as fair or poor most often (14.9%) among the occupation strata, followed by enlisted flyers (14.5%) and officers (7.7%). Of the participants who currently smoke and smoke 20 cigarettes or less per day, 19.9 percent reported their health as fair or poor. In contrast, 7.7 percent of participants who have never smoked reported their health as fair or poor. Participants who were the heaviest cigarette smokers across their lifetime (>10 pack-years) perceived their health as fair or poor more often than those who smoked less. The percentage for this category was 15.2 percent, whereas the percentage for participants in the moderate lifetime cigarette smoking category (>0-10 pack-years) was 10.8 percent. Of the participants who have never smoked, 7.7 percent rated their health as fair or poor.

Tests of associations for appearance of illness or distress revealed that race, current cigarette smoking, and lifetime cigarette smoking history were significant covariates (p=0.003, p=0.030, and p=0.027, respectively). The percentages of Blacks and non-Blacks that appeared ill or distressed were 4.7 and 1.2, respectively. Participants currently smoking more than 0, but up to 20 cigarettes per day, appeared ill or distressed most often (2.9%), followed by those in the more than 20 cigarettes per day category (2.2%), the former smoker category (1.3%), and never smoked category (0.5%). Percentages for lifetime cigarette smoking history were 2.1, 1.1, and 0.5 for the greater than 10 pack-years, the greater than 0 but no more than 10 pack-years, and the 0 pack-years categories, respectively.

For relative age appearance, significant covariate associations were found with occupation, current cigarette smoking, and lifetime cigarette smoking history (p=0.001 for each covariate). Enlisted flyers appearing older were 12.7 percent, while 11.0 and 5.6 percent of enlisted groundcrew and officers, respectively, appeared older. The percentage of current smokers appearing older in the greater than 20 cigarettes per day category was 25.6 percent, compared to only 3.9 percent for participants who had never smoked. The greater than 10 pack-years category of lifetime cigarette smoking history exhibited the highest percentage of participants that appeared older (13.2%). Nonsmokers exhibited the lowest percentage (3.9%).

The association tests for body fat in its continuous form revealed that current cigarette smoking, current alcohol use, and lifetime alcohol history were significant covariates (p<0.001, p<0.001, and p=0.022, respectively). For each analysis, each covariate was negatively associated with body fat (r=–0.187, r=–0.094, r=–0.050, respectively).

Significant results from the association tests for body fat in its discrete form were found among the following covariates: occupation, current cigarette smoking, lifetime cigarette smoking history, and current alcohol use (p=0.001, p=0.001, p=0.026, and p=0.003, respectively). For the occupation analysis, the percentages of participants classified as obese were 33.1 percent for enlisted groundcrew, 28.1 percent for enlisted flyers, and 25.3 percent for officers. Participants who were former smokers were classified as obese the most often (33.6%). Current smokers who smoke more than 20 cigarettes per day

exhibited the lowest percentage of obesity (19.0%). The analysis of lifetime cigarette smoking history revealed the highest proportion of obesity among participants in the greater than 0 but no more than 10 pack-years category (33.7%). Following were 28.1 percent for those in the greater than 10 pack-years category and 27.1 percent for nonsmokers. The current alcohol use analysis displayed the highest percentage of obesity (30.9%) for those participants who currently drink no more than 1 drink per day.

Analysis of erythrocyte sedimentation rate in its continuous form revealed significant associations with age, occupation, lifetime cigarette smoking history, and lifetime alcohol history ($p<0.001$, $p<0.001$, $p<0.001$, and $p=0.019$, respectively). Correlations with erythrocyte sedimentation rate were positive for age ($r=0.179$), lifetime cigarette smoking history ($r=0.155$), and lifetime alcohol history ($r=0.051$). Within the occupational strata, the mean erythrocyte sedimentation rate was 4.39 mm/hour for officers, 5.61 mm/hour for enlisted flyers, and 4.85 mm/hour for enlisted groundcrew.

Tests of association for erythrocyte sedimentation rate in its discrete form revealed that age, current cigarette smoking, and lifetime cigarette smoking history were significant covariates ($p=0.033$, $p=0.003$, and $p=0.002$, respectively). Older participants had a greater occurrence of high erythrocyte sedimentation rates (8.7%) than did younger participants (6.1%). Both current cigarette smoking and lifetime cigarette smoking history exhibited an increase in the percentage of abnormal erythrocyte sedimentation rates as the amount of cigarette smoking increased.

9.2.2 Exposure Analysis

The following section presents results of the statistical analyses of the dependent variables shown in Table 9-1. Dependent variables are grouped into three sections: (1) the Questionnaire Variable, derived from the questionnaire administered in the 1997 follow-up examination, (2) the Physical Examination Variables, obtained during the 1997 physical examination, and (3) the Laboratory Variable, derived from the laboratory portion of the 1997 follow-up examination.

Four models were examined for each dependent variable given in Table 9-1. The analyses of these models are presented below. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7, respectively. These analyses were performed both unadjusted and adjusted for relevant covariates. Model 1 examined the relation between the dependent variable and group (i.e., Ranch Hand or Comparison). In this model, exposure was defined as "yes" for Ranch Hands and "no" for Comparisons without regard to the magnitude of the exposure. As an attempt to quantify exposure, three contrasts of Ranch Hands and Comparisons were performed along with the overall Ranch Hand versus Comparison contrast. These three contrasts compared Ranch Hands and Comparisons within each occupational category (i.e., officers, enlisted flyers, and enlisted groundcrew). As described in previous reports and Table 2-8, the average levels of exposure to dioxin were highest for enlisted groundcrew, followed by enlisted flyers, and then officers.

Model 2 explored the relation between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 parts per trillion (ppt). If a participant did not have a 1987 dioxin level, a 1992 level was used to estimate the initial dioxin level. If a participant did not have a 1987 or a 1992 dioxin level, a 1997 level was used to estimate the initial dioxin level. A statistical adjustment for the percentage of body fat at the time of the participant's blood measurement of dioxin is included in this model to account for body-fat-related differences in elimination rate (58). This adjustment was accomplished for the unadjusted and adjusted analyses of all dependent variables except body fat in 1997. The use of body fat at the time of the participant's blood measurement of dioxin as a covariate masks the relation between body fat in 1997 and the dioxin measure.

Model 3 divided the Ranch Hands examined in Model 2 into two categories based on their initial dioxin measures. These two categories are referred to as "low Ranch Hand" and "high Ranch Hand." Two additional categories, Ranch Hands with 1987 serum dioxin levels at or below 10 ppt and Comparisons with 1987 serum dioxin levels at or below 10 ppt, were formed and included in the model. Ranch Hands with serum dioxin levels at or below 10 ppt are referred to as the "background Ranch Hand" category. Dioxin levels in 1992 were used if the 1987 levels were not available, and dioxin levels in 1997 were used if the 1987 and 1992 levels were not available. These four categories—Comparisons, background Ranch Hands, low Ranch Hands, and high Ranch Hands—were used in Model 3 analyses. The relation between the dependent variable in each of the three Ranch Hand categories and the dependent variable in the Comparison category was examined. A fourth contrast, exploring the relation of the dependent variable in the combined low and high Ranch Hand categories relative to Comparisons, also was conducted. This combination is referred to in the tables as the "low plus high Ranch Hand" category. As in Model 2, a statistical adjustment for the percentage of body fat at the time of the participant's blood measurement of dioxin was included in this model for the unadjusted and adjusted analyses of all dependent variables except body fat in 1997.

Model 4 examined the relation between the dependent variable and 1987 lipid-adjusted dioxin levels in all Ranch Hands with a dioxin measurement. If a participant did not have a 1987 dioxin measurement, the 1992 measurement was used to determine the dioxin level. If a participant did not have a 1987 or the 1992 dioxin measurement, a 1997 measurement was used to determine the dioxin level.

9.2.2.1 Questionnaire Variable

9.2.2.1.1 Self-perception of Health

The unadjusted and adjusted Model 1 analyses of self-perception of health revealed a significant difference between Ranch Hands and Comparisons across occupations (Table 9-3(a): Est. RR=1.44, p=0.007, and (b): Adj. RR=1.43, p=0.010, respectively). Unadjusted and adjusted differences within the enlisted groundcrew stratum also were significant (Table 9-3(a): Est. RR=1.50, p=0.028, and (b): Adj. RR=1.48, p=0.035, respectively). Ranch Hands perceived their health to be fair or poor more often than did Comparisons (i.e., 14.3% of Ranch Hands versus 10.4% of Comparisons overall).

Model 2 revealed a nonsignificant association between initial dioxin and self-perception of health for both the unadjusted and adjusted analyses (Table 9-3(c) and (d): p=0.859 and p=0.832, respectively).

The Model 3 unadjusted and adjusted analyses of self-perception of health revealed significant differences between Ranch Hands and Comparisons for the low Ranch Hand category (Table 9-3(e): Est. RR=1.77, p=0.005, and (f): Adj. RR=1.62, p=0.020, respectively) and the high Ranch Hand category (Table 9-3(e): Est. RR=2.14, p<0.001, and (f): Adj. RR=1.86, p=0.002, respectively). The low and high Ranch Hand categories combined were also significant in the unadjusted and adjusted analyses (Table 9-3(e): Est. RR=1.95, p<0.001, and (f): Adj. RR=1.74, p=0.001, respectively). Ranch Hands in the low and high dioxin categories perceived their health to be fair or poor more often than did Comparisons (i.e., 16.3% of Ranch Hands in the low dioxin category and 19.8% of Ranch Hands in the high dioxin category versus 9.8% of Comparisons).

The Model 4 unadjusted analysis revealed a significant relation between 1987 dioxin levels and self-perception of health (Table 9-3(g): Est. RR=1.22, p=0.002). The relation was marginally significant after adjustment for covariates (Table 9-3(h): p=0.079).

Table 9-3. Analysis of Self-perception of Health

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Fair or Poor	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***869***	***124 (14.3)***	***1.44 (1.10,1.87)***	***0.007***
	Comparison	***1,251***	***130 (10.4)***		
Officer	Ranch Hand	341	30 (8.8)	1.31 (0.78,2.18)	0.308
	Comparison	494	34 (6.9)		
Enlisted Flyer	Ranch Hand	151	26 (17.2)	1.48 (0.81,2.72)	0.203
	Comparison	187	23 (12.3)		
Enlisted Groundcrew	Ranch Hand	377	68 (18.0)	1.50 (1.05,2.15)	0.028
	Comparison	570	73 (12.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.43 (1.09,1.87)***	***0.010***
Officer	1.26 (0.75,2.12)	0.383
Enlisted Flyer	1.52 (0.82,2.82)	0.183
Enlisted Groundcrew	1.48 (1.03,2.14)	0.035

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Fair or Poor	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	25 (15.6)	1.02 (0.85,1.21)	0.859
Medium	162	35 (21.6)		
High	160	27 (16.9)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
477	0.98 (0.79,1.21)	0.832

[a] Relative risk for a twofold increase in initial dioxin.

Table 9-3. Analysis of Self-perception of Health (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Fair or Poor	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,213	119 (9.8)		
Background RH	380	34 (9.0)	0.97 (0.65,1.45)	0.880
Low RH	239	39 (16.3)	1.77 (1.19,2.62)	0.005
High RH	243	48 (19.8)	2.14 (1.48,3.10)	<0.001
Low plus High RH	482	87 (18.1)	1.95 (1.44,2.63)	<0.001

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,211		
Background RH	376	1.13 (0.75,1.72)	0.555
Low RH	237	1.62 (1.08,2.44)	0.020
High RH	240	1.86 (1.26,2.74)	0.002
Low plus High RH	477	1.74 (1.27,2.37)	0.001

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Fair or Poor	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	287	23 (8.0)	1.22 (1.08,1.39)	0.002
Medium	287	41 (14.3)		
High	288	57 (19.8)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 9-3. Analysis of Self-perception of Health (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
853	1.14 (0.98,1.32)	0.079

[a] Relative risk for a twofold increase in 1987 dioxin.

9.2.2.2 *Physical Examination Variables*

9.2.2.2.1 *Appearance of Illness or Distress as Assessed by Physician*

The unadjusted and adjusted analysis of appearance of illness or distress as assessed by a physician revealed nonsignificant differences between Ranch Hands and Comparisons (p>0.24 for each contrast) in the Model 1 analyses (Table 9-4(a) and (b)). Similarly, the analyses for Model 2 (Table 9-4(c) and (d)) and Model 4 (Table 9-4(g) and (h)) each revealed a nonsignificant relation between appearance of illness or distress as assessed by a physician and dioxin (both initial and 1987 levels; p>0.11 for all analyses).

Differences between Ranch Hands with low dioxin levels and Comparisons were significant in the Model 3 unadjusted analysis of appearance of illness or distress as assessed by a physician (Table 9-4(e): Est. RR=2.78, p=0.031). A significant difference also was found when the combination of low and high Ranch Hands was contrasted with Comparisons in the unadjusted analysis (Table 9-4(e): Est. RR=2.30, p=0.041). After adjustment for covariate effects, these contrasts were marginally significant for Ranch Hands with low dioxin levels (Table 9-4(f): p=0.092) and nonsignificant for the combination of low and high Ranch Hands (p=0.118). All other contrasts examined in the unadjusted and adjusted analyses of appearance of illness or distress as assessed by physician were nonsignificant (p>0.22 for each remaining contrast).

Table 9-4. Analysis of Appearance of Illness or Distress

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***870***	***15 (1.7)***	***1.55 (0.74,3.23)***	***0.242***
	Comparison	***1,251***	***14 (1.1)***		
Officer	Ranch Hand	341	3 (0.9)	1.09 (0.24,4.89)	0.913
	Comparison	494	4 (0.8)		
Enlisted Flyer	Ranch Hand	151	3 (2.0)	1.87 (0.31,11.37)	0.494
	Comparison	187	2 (1.1)		
Enlisted Groundcrew	Ranch Hand	378	9 (2.4)	1.71 (0.66,4.48)	0.272
	Comparison	570	8 (1.4)		

Table 9-4. Analysis of Appearance of Illness or Distress (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.44 (0.67,3.06)***	***0.350***
Officer	1.13 (0.25,5.16)	0.878
Enlisted Flyer	2.12 (0.33,13.61)	0.426
Enlisted Groundcrew	1.42 (0.52,3.89)	0.496

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	7 (4.4)	0.71 (0.42,1.20)	0.178
Medium	162	3 (1.9)		
High	160	2 (1.3)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
478	0.65 (0.36,1.15)	0.117

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,213	13 (1.1)		
Background RH	381	3 (0.8)	0.74 (0.21,2.63)	0.645
Low RH	239	7 (2.9)	2.78 (1.10,7.04)	0.031
High RH	243	5 (2.1)	1.92 (0.67,5.45)	0.223
Low plus High RH	482	12 (2.5)	2.30 (1.03,5.13)	0.041

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 9-4. Analysis of Appearance of Illness or Distress (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Comparison	1,211		
Background RH	378	0.76 (0.21,2.80)	0.684
Low RH	237	2.31 (0.87,6.11)	0.092
High RH	241	1.67 (0.54,5.19)	0.372
Low plus High RH	478	1.96 (0.84,4.58)	0.118

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			**Analysis Results for Log$_2$ (1987 Dioxin + 1)**	
1987 Dioxin	**n**	**Number (%) Yes**	**Estimated Relative Risk (95% C.I.)[a]**	**p-Value**
Low	288	3 (1.0)	1.09 (0.78,1.52)	0.631
Medium	287	7 (2.4)		
High	288	5 (1.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log$_2$ (1987 Dioxin + 1)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
856	1.05 (0.72,1.52)	0.800

[a] Relative risk for a twofold increase in 1987 dioxin.

9.2.2.2.2 Relative Age Appearance as Assessed by Physician

All unadjusted and adjusted analyses of relative age appearance as assessed by a physician were nonsignificant (Table 9-5: p>0.10 for each analysis) for Models 1 through 4.

Table 9-5. Analysis of Relative Age Appearance

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Older	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***870***	***90 (10.3)***	***1.27 (0.95,1.71)***	***0.112***
	Comparison	***1,251***	***104 (8.3)***		
Officer	Ranch Hand	341	22 (6.5)	1.29 (0.72,2.33)	0.392
	Comparison	494	25 (5.1)		
Enlisted Flyer	Ranch Hand	151	22 (14.6)	1.35 (0.71,2.56)	0.361
	Comparison	187	21 (11.2)		
Enlisted Groundcrew	Ranch Hand	378	46 (12.2)	1.22 (0.81,1.84)	0.337
	Comparison	570	58 (10.2)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.21 (0.88,1.65)***	***0.237***
Officer	1.29 (0.70,2.36)	0.410
Enlisted Flyer	1.28 (0.65,2.50)	0.476
Enlisted Groundcrew	1.14 (0.74,1.75)	0.550

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Older	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	17 (10.6)	1.05 (0.84,1.30)	0.694
Medium	162	16 (9.9)		
High	160	18 (11.3)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
478	1.01 (0.77,1.31)	0.962

[a] Relative risk for a twofold increase in initial dioxin.

Table 9-5. Analysis of Relative Age Appearance (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Older	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,213	102 (8.4)		
Background RH	381	39 (10.2)	1.25 (0.84,1.84)	0.271
Low RH	239	24 (10.0)	1.22 (0.76,1.94)	0.415
High RH	243	27 (11.1)	1.36 (0.87,2.13)	0.183
Low plus High RH	482	51 (10.6)	1.29 (0.90,1.83)	0.166

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,211		
Background RH	378	1.42 (0.93,2.16)	0.102
Low RH	237	1.11 (0.67,1.82)	0.691
High RH	241	1.05 (0.65,1.69)	0.857
Low plus High RH	478	1.08 (0.74,1.57)	0.706

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Older	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	33 (11.5)	0.97 (0.83,1.12)	0.654
Medium	287	25 (8.7)		
High	288	32 (11.1)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 9-5. Analysis of Relative Age Appearance (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
856	0.89 (0.75,1.05)	0.153

[a] Relative risk for a twofold increase in 1987 dioxin.

9.2.2.2.3 Body Fat (Continuous)

The Model 1 analyses of body fat in its continuous form revealed nonsignificant differences between Ranch Hands and Comparisons when examined across all occupations and within each occupation (Table 9-6(a,b): $p>0.31$ for each contrast).

The association between initial dioxin and body fat examined in the unadjusted Model 2 analyses also revealed marginally significant results (Table 9-6(c): $p=0.081$). After adjustment for covariate effects, this association became significant (Table 9-6(d): $p=0.020$). Body fat increased as initial dioxin levels increased.

Differences in mean body fat between Ranch Hands and Comparisons exhibited a dose-response relation in Model 3 analyses. As dioxin exposure increased, body fat also increased. The unadjusted and adjusted results are shown in Tables 9-6(e) and 9-6(f), respectively. Comparisons had a significantly higher body fat mean than did Background Ranch Hands ($p<0.001$ unadjusted and adjusted). The adjusted body fat mean of Ranch Hands in the low dioxin category was marginally significantly greater than Comparisons (Table 9-6(f): $p=0.052$). Ranch Hands in the high dioxin category had a significantly greater body fat mean than did Comparisons ($p=0.001$, unadjusted, and $p=0.002$, adjusted).

The Model 4 unadjusted and adjusted analyses each revealed a significant association between 1987 dioxin levels and body fat (Table 9-6(g): slope=0.046, $p<0.001$ and (h): adjusted slope=0.054, $p<0.001$). Body fat increased as dioxin levels increased. Adjusted body fat means for the low, medium, and high 1987 dioxin categories were 20.01 percent, 22.30 percent, and 23.60 percent, respectively.

Table 9-6. Analysis of Body Fat (Percent) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	**Group**	**n**	**Mean[a]**	**Difference of Means (95% C.I.)[b]**	**p-Value[c]**
All	***Ranch Hand***	***870***	***22.09***	***–0.19 --***	***0.436***
	Comparison	***1,251***	***22.28***		
Officer	Ranch Hand	341	22.04	0.17 --	0.656
	Comparison	494	21.87		
Enlisted Flyer	Ranch Hand	151	21.69	–0.51 --	0.390
	Comparison	187	22.20		
Enlisted Groundcrew	Ranch Hand	378	22.30	–0.37 --	0.318
	Comparison	570	22.67		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	**Group**	**n**	**Adjusted Mean[a]**	**Difference of Adj. Means (95% C.I.)[b]**	**p-Value[c]**
All	***Ranch Hand***	***863***	***22.13***	***–0.17 --***	***0.481***
	Comparison	***1,248***	***22.29***		
Officer	Ranch Hand	340	21.96	0.16 --	0.674
	Comparison	493	21.81		
Enlisted Flyer	Ranch Hand	149	21.84	–0.59 --	0.319
	Comparison	186	22.43		
Enlisted Groundcrew	Ranch Hand	374	22.45	–0.31 --	0.394
	Comparison	569	22.76		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 9-6. Analysis of Body Fat (Percent) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	160	22.75	0.006	0.015 (0.009)	0.081
Medium	162	23.46			
High	160	23.71			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of body fat versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	159	22.37	0.105	0.022 (0.010)	0.020
Medium	161	23.68			
High	158	23.88			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of body fat versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Mean[a]	Difference of Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,213	22.26		
Background RH	381	20.64	–1.62 --	<0.001
Low RH	239	23.04	0.78 --	0.045
High RH	243	23.57	1.31 --	0.001
Low plus High RH	482	23.30	1.04 --	0.001

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 9-6. Analysis of Body Fat (Percent) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,211	22.25		
Background RH	378	20.73	–1.52 --	<0.001
Low RH	237	23.00	0.75 --	0.052
High RH	241	23.51	1.26 --	0.002
Low plus High RH	478	23.26	1.01 --	0.001

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	288	20.35	0.072	0.046 (0.006)	<0.001
Medium	287	22.59			
High	288	23.45			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of body fat versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9-19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	287	20.01	0.155	0.054 (0.006)	<0.001
Medium	284	22.30			
High	285	23.60			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of body fat versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

9.2.2.2.4 Body Fat (Discrete)

All contrasts from the Models 1 and 2 unadjusted and adjusted analyses of body fat in its discrete form revealed nonsignificant differences between Ranch Hands and Comparisons (Table 9-7(a-d): p>0.17 for all contrasts).

Significantly fewer Ranch Hands in the Background category than Comparisons were obese (Table 9-7(e): Est. RR: 0.56, p<0.001 unadjusted, and Table 9-7(f): Adj. RR: 0.60, p=0.001 adjusted). Adjusted contrasts of Ranch Hands in the low dioxin category, and in the low and high dioxin categories combined, with Comparisons showed a marginally significantly higher percentage of obese Ranch Hands (Table 9-7(f): p=0.073 and p=0.097, respectively).

The Model 4 analyses revealed significant positive associations of body fat with 1987 dioxin levels, (Table 9-7(g): Est. RR=1.26, p<0.001, and (h): Adj. RR=1.29, p<0.001). Body fat increased as 1987 dioxin increased.

Table 9-7. Analysis of Body Fat (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Obese	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***870***	***244 (28.1)***	***0.91 (0.75,1.10)***	***0.316***
	Comparison	***1,251***	***376 (30.1)***		
Officer	Ranch Hand	341	88 (25.8)	1.05 (0.76,1.44)	0.767
	Comparison	494	123 (24.9)		
Enlisted Flyer	Ranch Hand	151	37 (24.5)	0.72 (0.45,1.17)	0.186
	Comparison	187	58 (31.0)		
Enlisted Groundcrew	Ranch Hand	378	119 (31.5)	0.88 (0.67,1.17)	0.382
	Comparison	570	195 (34.2)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.92 (0.75,1.11)***	***0.369***
Officer	1.05 (0.77,1.45)	0.754
Enlisted Flyer	0.71 (0.43,1.16)	0.173
Enlisted Groundcrew	0.89 (0.67,1.18)	0.431

Table 9-7. Analysis of Body Fat (Discrete) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Obese	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	160	55 (34.4)	1.00 (0.87,1.15)	0.989
Medium	162	59 (36.4)		
High	160	54 (33.8)		

[a] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
478	1.00 (0.85,1.19)	0.986

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Obese	Est. Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,213	361 (29.8)		
Background RH	381	73 (19.2)	0.56 (0.42,0.74)	<0.001
Low RH	239	85 (35.6)	1.30 (0.97,1.74)	0.076
High RH	243	83 (34.2)	1.22 (0.91,1.64)	0.175
Low plus High RH	482	168 (34.9)	1.26 (1.01,1.58)	0.042

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 9-7. Analysis of Body Fat (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,211		
Background RH	378	0.60 (0.45,0.80)	0.001
Low RH	237	1.31 (0.97,1.77)	0.073
High RH	241	1.12 (0.83,1.53)	0.451
Low plus High RH	478	1.21 (0.97,1.53)	0.097

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Obese	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	51 (17.7)	1.26 (1.14,1.40)	<0.001
Medium	287	90 (31.4)		
High	288	100 (34.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
856	1.29 (1.14,1.46)	<0.001

[a] Relative risk for a twofold increase in 1987 dioxin.

9.2.2.3 Laboratory Variable

9.2.2.3.1 Erythrocyte Sedimentation Rate (Continuous)

All analysis results from Models 1, 2, and 3 of erythrocyte sedimentation rate were nonsignificant (Table 9-8(a-f): p>0.17 for each analysis). The Model 4 analysis revealed a significant association between erythrocyte sedimentation rate and 1987 dioxin levels for both the unadjusted and adjusted analyses (Table 9-8(g): p=0.004, and (h): p=0.037, respectively). Erythrocyte sedimentation rate increased as

dioxin increased in these analyses. Adjusted erythrocyte sedimentation rate means for the low, medium, and high 1987 dioxin categories were 4.34 mm/hr, 4.62 mm/hr, and 5.29 mm/hr, respectively.

Table 9-8. Analysis of Erythrocyte Sedimentation Rate (mm/hr) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***870***	***4.82***	***0.09 --***	***0.680***
	Comparison	***1,251***	***4.74***		
Officer	Ranch Hand	341	4.36	–0.05 --	0.873
	Comparison	494	4.41		
Enlisted Flyer	Ranch Hand	151	5.35	–0.47 --	0.429
	Comparison	187	5.83		
Enlisted Groundcrew	Ranch Hand	378	5.06	0.35 --	0.263
	Comparison	570	4.71		

[a] Transformed from natural logarithm scale of erythrocyte sedimentation rate + 0.1.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale of erythrocyte sedimentation rate + 0.1.
[c] P-value is based on difference of means on natural logarithm scale of erythrocyte sedimentation rate + 0.1.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	Ranch Hand	860	5.12	0.04 --	0.850
	Comparison	1,248	5.08		
Officer	Ranch Hand	339	4.30	–0.08 --	0.789
	Comparison	493	4.38		
Enlisted Flyer	Ranch Hand	148	5.13	–0.60 --	0.286
	Comparison	186	5.74		
Enlisted Groundcrew	Ranch Hand	373	5.81	0.42 --	0.236
	Comparison	569	5.39		

[a] Transformed from natural logarithm scale of erythrocyte sedimentation rate + 0.1.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale of erythrocyte sedimentation rate + 0.1.
[c] P-value is based on difference of means on natural logarithm scale of erythrocyte sedimentation rate + 0.1.

Table 9-8. Analysis of Erythrocyte Sedimentation Rate (mm/hr) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	160	4.70	4.74	0.009	0.029 (0.034)	0.387
Medium	162	5.99	6.00			
High	160	5.04	4.99			

[a] Transformed from natural logarithm scale of erythrocyte sedimentation rate + 0.1.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of erythrocyte sedimentation rate + 0.1 versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	159	4.45	0.086	0.041 (0.039)	0.289
Medium	160	5.66			
High	158	4.83			

[a] Transformed from natural logarithm scale of erythrocyte sedimentation rate + 0.1.
[b] Slope and standard error based on natural logarithm of erythrocyte sedimentation rate + 0.1 versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,213	4.75	4.74		
Background RH	381	4.31	4.48	–0.26 --	0.323
Low RH	239	5.12	5.06	0.32 --	0.350
High RH	243	5.32	5.12	0.38 --	0.259
Low plus High RH	482	5.22	5.09	0.35 --	0.176

[a] Transformed from natural logarithm scale of erythrocyte sedimentation rate + 0.1.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale of erythrocyte sedimentation rate + 0.1.
[d] P-value is based on difference of means on natural logarithm scale of erythrocyte sedimentation rate + 0.1.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 9-8. Analysis of Erythrocyte Sedimentation Rate (mm/hr) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,211	5.12		
Background RH	376	4.92	–0.20 --	0.484
Low RH	237	5.12	0.00 --	0.992
High RH	240	5.48	0.36 --	0.322
Low plus High RH	477	5.29	0.17 --	0.510

[a] Transformed from natural logarithm scale of erythrocyte sedimentation rate + 0.1.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale of erythrocyte sedimentation rate + 0.1.
[c] P-value is based on difference of means on natural logarithm scale of erythrocyte sedimentation rate + 0.1.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)[b]		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	288	4.20	0.009	0.063 (0.022)	0.004
Medium	287	4.81			
High	288	5.46			

[a] Transformed from natural logarithm scale of erythrocyte sedimentation rate + 0.1.
[b] Slope and standard error based on natural logarithm of erythrocyte sedimentation rate + 0.1 versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	285	4.34	0.088	0.052 (0.025)	0.037
Medium	284	4.62			
High	284	5.29			

[a] Transformed from natural logarithm scale of erythrocyte sedimentation rate + 0.1.
[b] Slope and standard error based on natural logarithm of erythrocyte sedimentation rate + 0.1 versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

9.2.2.3.2 *Erythrocyte Sedimentation Rate (Discrete)*

Similar to the continuous analyses, all results from the analyses of erythrocyte sedimentation rate in its discrete form in Models 1, 2, and 3 were nonsignificant (Table 9-9(a–f): p>0.13). The Model 4 unadjusted analysis revealed a significant association between erythrocyte sedimentation rate and 1987 dioxin levels (Table 9-9(g): Est. RR=1.18, p=0.040). After adjustment for covariates, this association was nonsignificant (Table 9-9(h): p=0.169).

Table 9-9. Analysis of Erythrocyte Sedimentation Rate (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***870***	***72 (8.3)***	***1.19 (0.86,1.65)***	***0.289***
	Comparison	***1,251***	***88 (7.0)***		
Officer	Ranch Hand	341	20 (5.9)	0.84 (0.48,1.49)	0.557
	Comparison	494	34 (6.9)		
Enlisted Flyer	Ranch Hand	151	17 (11.3)	1.57 (0.75,3.29)	0.235
	Comparison	187	14 (7.5)		
Enlisted Groundcrew	Ranch Hand	378	35 (9.3)	1.35 (0.84,2.17)	0.212
	Comparison	570	40 (7.0)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.17 (0.84,1.63)***	***0.356***
Officer	0.86 (0.48,1.53)	0.602
Enlisted Flyer	1.59 (0.75,3.38)	0.231
Enlisted Groundcrew	1.29 (0.79,2.10)	0.305

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	11 (6.9)	1.17 (0.93,1.46)	0.179
Medium	162	19 (11.7)		
High	160	15 (9.4)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 9-9. Analysis of Erythrocyte Sedimentation Rate (Discrete) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
477	1.23 (0.94,1.62)	0.138

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,213	85 (7.0)		
Background RH	381	25 (6.6)	1.03 (0.65,1.64)	0.908
Low RH	239	21 (8.8)	1.25 (0.75,2.06)	0.392
High RH	243	24 (9.9)	1.34 (0.83,2.16)	0.236
Low plus High RH	482	45 (9.3)	1.29 (0.88,1.89)	0.190

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,211		
Background RH	376	1.07 (0.66,1.73)	0.777
Low RH	237	1.04 (0.61,1.75)	0.897
High RH	240	1.36 (0.82,2.26)	0.237
Low plus High RH	477	1.19 (0.80,1.77)	0.398

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 9-9. Analysis of Erythrocyte Sedimentation Rate (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	19 (6.6)	1.18 (1.01,1.39)	0.040
Medium	287	23 (8.0)		
High	288	28 (9.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
853	1.14 (0.94,1.38)	0.169

[a] Relative risk for a twofold increase in 1987 dioxin.

9.2.3 Longitudinal Analysis

Longitudinal analyses were conducted on five variables—self-perception of health, appearance of illness or distress, relative age, body fat, and erythrocyte sedimentation rate—to examine whether changes across time differed with respect to group membership (Model 1), initial dioxin (Model 2), and categorized dioxin (Model 3). Model 4 was not examined in longitudinal analyses because 1987 dioxin, the measure of exposure in these models, changes over time and is not available for all participants for 1982 or 1997.

Discrete analyses were performed for all variables, and continuous analyses were additionally performed for body fat and erythrocyte sedimentation rate. The longitudinal analyses for all of these variables investigated the difference between the 1982 examination and the 1997 examination. These analyses were used to investigate the temporal effects of dioxin during the 15-year period between 1982 and 1997.

The cutpoints for abnormal erythrocyte sedimentation rate differed by examination date and age. For the 1982 baseline examination, the cutpoint was 12 mm/hr for all participants. For the 1985, 1987, and 1992 follow-up examinations, the cutpoint was 15 mm/hr for participants younger than 50 and 20 mm/hr for participants at least 50 years old at the time of the examination.

Participants who were abnormal in 1982 were not included in the longitudinal analysis of discrete dependent variables. The purpose of the longitudinal analysis was to examine the effects of dioxin exposure across time. Participants who were abnormal in 1982 were not considered to be at risk for developing the condition, because the condition already existed at the time of the first collection of data for the AFHS (1982). Only participants who were normal at the 1982 examination were considered to be at risk for developing the condition; therefore, the rate of abnormalities under this restriction approximates an incidence rate between 1982 and 1997. That is, an incidence rate is a measure of the

rate at which people without a condition develop the condition during a specified period of time (86). Summary statistics are provided for reference purposes for the 1985, 1987, and 1992 examinations.

The longitudinal analyses for the discrete variables examined relative risks at the 1997 examination for participants who were classified as normal at the 1982 examination. The adjusted relative risks estimated from each of the three models were used to investigate the change in the dependent variable over time. All three models were adjusted for age; Models 2 and 3 also were adjusted for the percentage of body fat at the time of the blood measurement of dioxin. This was accomplished for all dependent variables except body fat in 1997. As described previously, the use of body fat at the time of the participant's blood measurement of dioxin as a covariate masks the relation between body fat in 1997 and the dioxin measure.

The longitudinal analysis for the two continuous variables examined the paired difference between the measurements from 1982 and 1997. These paired differences measured the change in body fat or erythrocyte sedimentation rate over time. Each of the three models used in the longitudinal analysis was adjusted for age and the dependent variable as measured in 1982 (see Chapter 7, Statistical Methods). The analyses of Models 2 and 3 for erythrocyte sedimentation rate also were adjusted for percent body fat at the time of the blood measurement of dioxin. A logarithmic transformation was applied to both of these variables for analytic purposes.

9.2.3.1 Questionnaire Variable

9.2.3.1.1 Self-perception of Health

Longitudinal analyses were conducted for the examination of participant's self-perception of health in 1997. Only participants who reported their health as excellent or good in 1982 were included in the analysis. Results from analyses of all three models are found in Table 9-10 and indicate no significant associations between self-perception of health and any of the three measures of dioxin exposure (group status, initial dioxin, or categorized dioxin: $p>0.11$ for each contrast).

Table 9-10. Longitudinal Analysis of Self-perception of Health

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) Fair or Poor/(n) Examination 1982	1985	1987	1992	1997
All	***Ranch Hand***	***152 (18.7) (813)***	***62 (7.8) (795)***	***43 (5.5) (788)***	***67 (8.5) (792)***	***117 (14.4) (813)***
	Comparison	***129 (13.2) (974)***	***53 (5.5) (956)***	***42 (4.4) (949)***	***59 (6.2) (952)***	***103 (10.6) (974)***
Officer	Ranch Hand	33 (10.7) (309)	11 (3.6) (305)	12 (4.0) (302)	14 (4.6) (305)	28 (9.1) (309)
	Comparison	35 (9.2) (379)	13 (3.5) (373)	7 (1.9) (367)	16 (4.3) (374)	26 (6.9) (379)
Enlisted Flyer	Ranch Hand	31 (21.1) (147)	6 (4.2) (144)	6 (4.2) (142)	13 (9.0) (144)	24 (16.3) (147)
	Comparison	22 (15.2) (145)	9 (6.3) (144)	4 (2.8) (143)	10 (7.0) (143)	16 (11.0) (145)
Enlisted Groundcrew	Ranch Hand	88 (24.7) (357)	45 (13.0) (346)	25 (7.3) (344)	40 (11.7) (343)	65 (18.2) (357)
	Comparison	72 (16.0) (450)	31 (7.1) (439)	31 (7.1) (439)	33 (7.6) (435)	61 (13.6) (450)

Occupational Category	Group	Excellent or Good in 1982: n in 1997	Number (%) Fair or Poor in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***661***	***49 (7.4)***	***1.07 (0.72,1.58)***	***0.746***
	Comparison	***845***	***59 (7.0)***		
Officer	Ranch Hand	276	13 (4.7)	1.01 (0.48,2.14)	0.978
	Comparison	344	16 (4.7)		
Enlisted Flyer	Ranch Hand	116	10 (8.6)	1.37 (0.52,3.60)	0.526
	Comparison	123	8 (6.5)		
Enlisted Groundcrew	Ranch Hand	269	26 (9.7)	1.08 (0.63,1.84)	0.783
	Comparison	378	35 (9.3)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had an excellent or good self-perception of health in 1982 (see Chapter 7, Statistical Methods).

Table 9-10. Longitudinal Analysis of Self-perception of Health (Continued)

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN

Initial Dioxin	Number (%) Fair or Poor/(n) Examination 1982	1985	1987	1992	1997
Low	25 (16.3) (153)	14 (9.3) (150)	8 (5.3) (152)	13 (8.8) (148)	24 (15.7) (153)
Medium	40 (25.3) (158)	15 (9.7) (155)	11 (7.1) (155)	20 (12.9) (155)	34 (21.5) (158)
High	27 (17.8) (152)	20 (13.4) (149)	9 (6.1) (147)	16 (10.7) (149)	25 (16.5) (152)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Excellent or Good in 1982			
Initial Dioxin	n in 1997	Number (%) Fair or Poor in 1997	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	128	9 (7.0)	0.89 (0.66,1.20)	0.440
Medium	118	17 (14.4)		
High	125	9 (7.2)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had an excellent or good self-perception of health in 1982 (see Chapter 7, Statistical Methods).

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY

Dioxin Category	Number (%) Fair or Poor/(n) Examination 1982	1985	1987	1992	1997
Comparison	122 (12.9) (946)	51 (5.5) (931)	40 (4.3) (923)	54 (5.8) (925)	93 (9.8) (946)
Background RH	57 (16.6) (344)	13 (3.9) (336)	14 (4.3) (329)	17 (5.1) (335)	31 (9.0) (344)
Low RH	44 (19.2) (229)	22 (9.9) (223)	15 (6.6) (226)	20 (9.0) (222)	38 (16.6) (229)
High RH	48 (20.5) (234)	27 (11.7) (231)	13 (5.7) (228)	29 (12.6) (230)	45 (19.2) (234)
Low plus High RH	92 (19.9) (463)	49 (10.8) (454)	28 (6.2) (454)	49 (10.8) (452)	83 (17.9) (463)

Table 9-10. Longitudinal Analysis of Self-perception of Health (Continued)

Dioxin Category	Excellent or Good in 1982: n in 1997	Excellent or Good in 1982: Number (%) Fair or Poor in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	824	53 (6.4)		
Background RH	287	13 (4.5)	0.74 (0.39,1.38)	0.339
Low RH	185	16 (8.7)	1.32 (0.74,2.38)	0.349
High RH	186	19 (10.2)	1.56 (0.89,2.75)	0.119
Low plus High RH	371	35 (9.4)	1.44 (0.92,2.26)	0.113

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had an excellent or good self-perception of health in 1982 (see Chapter 7, Statistical Methods).

9.2.3.2 Physical Examination Variables

9.2.3.2.1 Appearance of Illness or Distress

Longitudinal analyses were conducted on participants in the 1997 follow-up who did not appear ill or distressed in 1982. The results revealed no significant differences between Ranch Hands and Comparisons in the percentage of participants that appeared ill or distressed, either when examined across all occupations or within each occupational category (Table 9-11(a): p>0.19 for each contrast). Analyses that examined the effect of initial dioxin on appearance of illness or distress also were nonsignificant (Table 9-11(b): p=0.132). A statistically significant difference in the appearance of illness or distress between Ranch Hands in the low dioxin category and Comparisons was found, with a greater percentage of Ranch Hands appearing ill or distressed (Table 9-11(c): Adj. RR=3.07, p=0.029). The relative risk estimate remained significant when Ranch Hands from the low and high dioxin categories were combined (Adj. RR=2.50, p=0.049). Other contrasts of Ranch Hands and Comparisons were nonsignificant (p>0.24 for each remaining contrast).

Table 9-11. Longitudinal Analysis of Appearance of Illness or Distress

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) Yes/(n) Examination 1982	1985	1987	1992	1997
All	***Ranch Hand***	***5 (0.6)***	***2 (0.3)***	***2 (0.3)***	***16 (2.0)***	***14 (1.7)***
		(817)	***(797)***	***(791)***	***(795)***	***(817)***
	Comparison	***1 (0.1)***	***3 (0.3)***	***2 (0.2)***	***13 (1.4)***	***9 (0.9)***
		(974)	***(956)***	***(948)***	***(954)***	***(974)***
Officer	Ranch Hand	3 (1.0)	1 (0.3)	1 (0.3)	8 (2.6)	3 (1.0)
		(312)	(308)	(305)	(307)	(312)
	Comparison	0 (0.0)	0 (0.0)	0 (0.0)	4 (1.1)	3 (0.8)
		(380)	(374)	(368)	(375)	(380)
Enlisted Flyer	Ranch Hand	0 (0.0)	1 (0.7)	0 (0.0)	3 (2.1)	3 (2.0)
		(148)	(145)	(143)	(145)	(148)
	Comparison	1 (0.7)	2 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)
		(144)	(143)	(142)	(142)	(144)
Enlisted Groundcrew	Ranch Hand	2 (0.6)	0 (0.0)	1 (0.3)	5 (1.5)	8 (2.2)
		(357)	(344)	(343)	(343)	(357)
	Comparison	0 (0.0)	1 (0.2)	2 (0.5)	9 (2.1)	6 (1.3)
		(450)	(439)	(438)	(437)	(450)

Occupational Category	Group	No in 1982 n in 1997	Number (%) Yes in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[b]
All	***Ranch Hand***	***812***	***13 (1.6)***	***1.75 (0.74,4.11)***	***0.196***
	Comparison	***973***	***9 (0.9)***		
Officer	Ranch Hand	309	2 (0.7)	0.82 (0.14,4.95)	0.829
	Comparison	380	3 (0.8)		
Enlisted Flyer	Ranch Hand	148	3 (2.0)	--	0.258[b]
	Comparison	143	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	355	8 (2.3)	1.81 (0.62,5.28)	0.280
	Comparison	450	6 (1.3)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1997 results; results adjusted for age in 1997.
[b] P-value determined using a chi-square test with continuity correction because of the sparse number of participants appearing ill or distressed.
--: Results not presented because of the sparse number of participants appearing ill or distressed.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who did not appear ill or distressed in 1982 (see Chapter 7, Statistical Methods).

Table 9-11. Longitudinal Analysis of Appearance of Illness or Distress (Continued)

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN					
	Number (%) Yes/(n) Examination				
Initial Dioxin	1982	1985	1987	1992	1997
Low	0 (0.0) (154)	0 (0.0) (151)	0 (0.0) (153)	3 (2.0) (149)	7 (4.6) (154)
Medium	0 (0.0) (158)	1 (0.7) (154)	0 (0.0) (155)	4 (2.6) (155)	3 (1.9) (158)
High	2 (1.3) (152)	0 (0.0) (148)	1 (0.7) (147)	1 (0.7) (149)	1 (0.7) (152)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	No in 1982			
Initial Dioxin	n in 1997	Number (%) Yes in 1997	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	154	7 (4.6)	0.65 (0.35,1.20)	0.132
Medium	158	3 (1.9)		
High	150	1 (0.7)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who did not appear ill or distressed in 1982 (see Chapter 7, Statistical Methods).

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY					
	Number (%) Yes/(n) Examination				
Dioxin Category	1982	1985	1987	1992	1997
Comparison	1 (0.1) (946)	3 (0.3) (931)	2 (0.2) (922)	12 (1.3) (927)	9 (1.0) (946)
Background RH	3 (0.9) (347)	1 (0.3) (339)	1 (0.3) (331)	7 (2.1) (337)	3 (0.9) (347)
Low RH	0 (0.0) (229)	1 (0.5) (223)	0 (0.0) (226)	5 (2.3) (222)	7 (3.1) (229)
High RH	2 (0.9) (235)	0 (0.0) (230)	1 (0.4) (229)	3 (1.3) (231)	4 (1.7) (235)
Low plus High RH	2 (0.4) (464)	1 (0.2) (453)	1 (0.2) (455)	8 (1.8) (453)	11 (2.4) (464)

Table 9-11. Longitudinal Analysis of Appearance of Illness or Distress (Continued)

Dioxin Category	No in 1982: n in 1997	No in 1982: Number (%) Yes in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	945	9 (1.0)		
Background RH	344	2 (0.6)	0.59 (0.13,2.77)	0.507
Low RH	229	7 (3.1)	3.07 (1.12,8.36)	0.029
High RH	233	4 (1.7)	2.04 (0.61,6.83)	0.246
Low plus High RH	462	11 (2.4)	2.50 (1.00,6.22)	0.049

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who did not appear ill or distressed in 1982 (see Chapter 7, Statistical Methods).

9.2.3.2.2 Relative Age Appearance

The 1997 longitudinal analyses of relative age appearance were conducted among participants who appeared the same or younger than their chronological age in 1982. The associations from all analyses of relative age appearance and dioxin exposure were nonsignificant (Table 9-12: p>0.26 for each analysis).

Table 9-12. Longitudinal Analysis of Relative Age Appearance

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) Older/(n) Examination 1982	1985	1987	1992	1997
All	***Ranch Hand***	***15 (1.8) (819)***	***25 (3.1) (800)***	***39 (4.9) (793)***	***40 (5.0) (797)***	***82 (10.0) (819)***
	Comparison	***19 (2.0) (974)***	***35 (3.7) (956)***	***40 (4.2) (949)***	***54 (5.7) (954)***	***82 (8.4) (974)***
Officer	Ranch Hand	2 (0.6) (312)	4 (1.3) (308)	8 (2.6) (305)	7 (2.3) (307)	19 (6.1) (312)
	Comparison	3 (0.8) (379)	1 (0.3) (373)	8 (2.2) (367)	13 (3.5) (374)	19 (5.0) (379)
Enlisted Flyer	Ranch Hand	0 (0.0) (148)	3 (2.1) (145)	11 (7.7) (143)	13 (9.0) (145)	22 (14.9) (148)
	Comparison	4 (2.8) (145)	12 (8.3) (144)	11 (7.7) (143)	8 (5.6) (143)	17 (11.7) (145)
Enlisted Groundcrew	Ranch Hand	13 (3.6) (359)	18 (5.2) (347)	20 (5.8) (345)	20 (5.8) (345)	41 (11.4) (359)
	Comparison	12 (2.7) (450)	22 (5.0) (439)	21 (4.8) (439)	33 (7.6) (437)	46 (10.2) (450)

Occupational Category	Group	As Old As or Younger in 1982: n in 1997	Number (%) Older in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***804***	***76 (9.5)***	***1.21 (0.87,1.69)***	***0.265***
	Comparison	***955***	***76 (8.0)***		
Officer	Ranch Hand	310	19 (6.1)	1.22 (0.63,2.35)	0.554
	Comparison	376	19 (5.1)		
Enlisted Flyer	Ranch Hand	148	22 (14.9)	1.35 (0.68,2.70)	0.390
	Comparison	141	16 (11.4)		
Enlisted Groundcrew	Ranch Hand	346	35 (10.1)	1.12 (0.70,1.81)	0.637
	Comparison	438	41 (9.4)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who appeared as old as or younger than their age in 1982 (see Chapter 7, Statistical Methods).

Table 9-12. Longitudinal Analysis of Relative Age Appearance (Continued)

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN

	Number (%) Older/(n) Examination				
Initial Dioxin	**1982**	**1985**	**1987**	**1992**	**1997**
Low	2 (1.3) (154)	5 (3.3) (151)	8 (5.2) (153)	6 (4.0) (149)	16 (10.4) (154)
Medium	2 (1.3) (159)	5 (3.2) (156)	6 (3.9) (156)	9 (5.8) (156)	16 (10.1) (159)
High	5 (3.3) (153)	9 (6.0) (149)	7 (4.7) (148)	9 (6.0) (150)	15 (9.8) (153)

Initial Dioxin Category Summary Statistics As Old As or Younger in 1982			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	**n in 1997**	**Number (%) Older in 1997**	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**
Low	152	15 (9.9)	1.04 (0.81,1.33)	0.765
Medium	157	16 (10.2)		
High	148	13 (8.8)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who appeared as old as or younger than their age in 1982 (see Chapter 7, Statistical Methods).

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY

	Number (%) Older/(n) Examination				
Dioxin Category	**1982**	**1985**	**1987**	**1992**	**1997**
Comparison	19 (2.0) (946)	35 (3.8) (931)	40 (4.3) (923)	53 (5.7) (927)	81 (8.6) (946)
Background RH	6 (1.7) (347)	6 (1.8) (339)	18 (5.4) (331)	15 (4.5) (337)	35 (10.1) (347)
Low RH	2 (0.9) (230)	7 (3.1) (224)	8 (3.5) (227)	7 (3.1) (223)	23 (10.0) (230)
High RH	7 (3.0) (236)	12 (5.2) (232)	13 (5.7) (230)	17 (7.3) (232)	24 (10.2) (236)
Low plus High RH	9 (1.9) (466)	19 (4.2) (456)	21 (4.6) (457)	24 (5.3) (455)	47 (10.1) (466)

Table 9-12. Longitudinal Analysis of Relative Age Appearance (Continued)

	As Old As or Younger in 1982			
Dioxin Category	n in 1997	Number (%) Older in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	927	75 (8.1)		
Background RH	341	32 (9.4)	1.14 (0.74,1.77)	0.545
Low RH	228	22 (9.7)	1.19 (0.72,1.97)	0.487
High RH	229	22 (9.6)	1.28 (0.77,2.12)	0.339
Low plus High RH	457	44 (9.6)	1.24 (0.84,1.83)	0.289

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who appeared as old as or younger than their age in 1982 (see Chapter 7, Statistical Methods).

9.2.3.2.3 Body Fat (Continuous)

Longitudinal analyses that examined the mean difference between body fat in 1982 and 1997 were performed to explore associations with group and dioxin. The results of the longitudinal analyses are seen in Table 9-13.

No significant associations were observed between group status (Ranch Hand, Comparison) and the change in body fat over the 15 years of the study, either across or within occupational strata (Table 9-13(a): $p>0.40$ for all analyses). In addition, no significant associations were observed between change in body fat and categorized dioxin (Table 9-13(c): $p>0.19$ for all analyses).

A significant negative association was observed between the change in body fat and initial dioxin (Table 9-13(b): $p=0.049$). The mean body fat percentages increased between 1982 and 1997 for all initial dioxin categories. The increase was greater for those participants with lesser amounts of initial dioxin exposure.

Table 9-13. Longitudinal Analysis of Body Fat (Percent) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS									
		Mean[a]/(n) Examination							
Occupational Category	Group	1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	***Ranch Hand***	***19.82 (817)***	***20.70 (799)***	***21.07 (791)***	***21.88 (795)***	***22.11 (817)***	***2.29***	***–0.01***	***0.938***
	Comparison	***19.94 (976)***	***21.00 (958)***	***21.24 (951)***	***22.11 (956)***	***22.24 (976)***	***2.30***		
Officer	Ranch Hand	20.09 (311)	20.93 (307)	21.22 (304)	21.85 (306)	22.06 (311)	1.98	0.07	0.715
	Comparison	19.86 (380)	20.88 (374)	20.99 (368)	21.70 (375)	21.77 (380)	1.91		
Enlisted Flyer	Ranch Hand	19.48 (147)	20.47 (144)	20.67 (142)	21.43 (144)	21.65 (147)	2.17	–0.34	0.403
	Comparison	19.56 (145)	20.35 (144)	20.69 (143)	21.56 (143)	22.07 (145)	2.51		
Enlisted Groundcrew	Ranch Hand	19.74 (359)	20.59 (348)	21.10 (345)	22.10 (345)	22.35 (359)	2.61	0.05	0.997
	Comparison	20.14 (451)	21.32 (440)	21.64 (440)	22.65 (438)	22.70 (451)	2.56		

[a] Transformed from natural logarithm scale.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of natural logarithm of body fat; results adjusted for natural logarithm of body fat in 1982 and age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

Table 9-13. Longitudinal Analysis of Body Fat (Percent) (Continuous) (Continued)

(b) MODEL 2: RANCH HANDS – INITIAL DIOXIN							
Initial Dioxin Category Summary Statistics						Analysis Results for Log_2 (Initial Dioxin)[b]	
	Mean[a]/(n) Examination						
Initial Dioxin	1982	1985	1987	992	1997	Adjusted Slope (Std. Error)	p-Value
Low	20.23 (154)	21.27 (151)	21.56 (153)	22.60 (149)	22.66 (154)	–0.012 (0.006)	0.049
Medium	20.89 (157)	21.97 (154)	22.26 (154)	22.97 (154)	23.48 (157)		
High	21.70 (153)	22.56 (150)	22.97 (148)	23.65 (150)	23.80 (153)		

[a] Transformed from natural logarithm scale.
[b] Results based on difference between natural logarithm of 1997 body fat and natural logarithm of 1982 body fat versus $\log_2$ (initial dioxin); results adjusted for natural logarithm of 1982 body fat and age in 1997.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

Table 9-13. Longitudinal Analysis of Body Fat (Percent) (Continuous) (Continued)

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY								
Dioxin Category	Mean[a]/(n) Examination 1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
Comparison	19.90 (948)	20.96 (933)	21.20 (925)	22.07 (929)	22.21 (948)	2.31		
Background RH	18.39 (347)	19.13 (339)	19.52 (331)	20.35 (337)	20.58 (347)	2.19	–0.12	0.708
Low RH	20.43 (230)	21.46 (224)	21.72 (227)	22.70 (223)	22.96 (230)	2.53	0.22	0.193
High RH	21.43 (234)	22.38 (231)	22.79 (228)	23.44 (230)	23.66 (234)	2.22	–0.09	0.322
Low plus High RH	20.93 (464)	21.92 (455)	22.25 (455)	23.07 (453)	23.31 (464)	2.38	0.07	0.853

[a] Transformed from natural logarithm scale.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of natural logarithm of body fat; results adjusted for body fat in 1982 and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

9.2.3.2.4 Body Fat (Discrete)

Body fat in its discrete form was analyzed across time for participants in 1997 who were considered lean or normal in 1982. The differences in percentages of obese participants for Ranch Hands and Comparisons were nonsignificant (Table 9-14(a): p>0.25 for each contrast). A marginally significant association between initial dioxin and body fat was revealed (Table 9-14(b): p=0.069). The contrast examining differences in obesity between Ranch Hands in the Background dioxin category and Comparisons also revealed a significant result (Table 9-14(c): Adj. RR=0.64, p=0.014), with less Ranch Hands being obese in 1997. All other contrasts of Ranch Hands and Comparisons in the analyses of dioxin categories were nonsignificant (p>0.15 for each remaining contrast).

Table 9-14. Longitudinal Analysis of Body Fat (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS						
		Number (%) Obese/(n) Examination				
Occupational Category	Group	1982	1985	1987	1992	1997
All	***Ranch Hand***	***108 (13.2) (817)***	***148 (18.5) (799)***	***158 (20.0) (791)***	***202 (25.4) (795)***	***229 (28.0) (817)***
	Comparison	***138 (14.1) (976)***	***191 (19.9) (958)***	***208 (21.9) (951)***	***256 (26.8) (956)***	***293 (30.0) (976)***
Officer	Ranch Hand	36 (11.6) (311)	57 (18.6) (307)	56 (18.4) (304)	72 (23.5) (306)	81 (26.1) (311)
	Comparison	38 (10.0) (380)	56 (15.0) (374)	62 (16.9) (368)	88 (23.5) (375)	89 (23.4) (380)
Enlisted Flyer	Ranch Hand	15 (10.2) (147)	21 (14.6) (144)	25 (17.6) (142)	30 (20.8) (144)	36 (24.5) (147)
	Comparison	19 (13.1) (145)	25 (17.4) (144)	25 (17.5) (143)	31 (21.7) (143)	43 (29.7) (145)
Enlisted Groundcrew	Ranch Hand	57 (15.9) (359)	70 (20.1) (348)	77 (22.3) (345)	100 (29.0) (345)	112 (31.2) (359)
	Comparison	81 (18.0) (451)	110 (25.0) (440)	121 (27.5) (440)	137 (31.3) (438)	161 (35.7) (451)

		Lean or Normal in 1982			
Occupational Category	Group	n in 1997	Number (%) Obese in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***709***	***136 (19.2)***	***0.93 (0.72,1.20)***	***0.567***
	Comparison	***838***	***170 (20.3)***		
Officer	Ranch Hand	275	52 (18.9)	1.19 (0.79,1.81)	0.403
	Comparison	342	56 (16.4)		
Enlisted Flyer	Ranch Hand	132	22 (16.7)	0.81 (0.43,1.52)	0.512
	Comparison	126	25 (19.8)		
Enlisted Groundcrew	Ranch Hand	302	62 (20.5)	0.81 (0.56,1.17)	0.253
	Comparison	370	89 (24.1)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who were lean or had normal body fat in 1982 (see Chapter 7, Statistical Methods).

Table 9-14. Longitudinal Analysis of Body Fat (Discrete) (Continued)

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN					
	Number (%) Obese/(n) Examination				
Initial Dioxin	1982	1985	1987	1992	1997
Low	21 (13.6) (154)	31 (20.5) (151)	33 (21.6) (153)	40 (26.9) (149)	51 (33.1) (154)
Medium	27 (17.2) (157)	41 (26.6) (154)	43 (27.9) (154)	55 (35.7) (154)	57 (36.3) (157)
High	31 (20.3) (153)	40 (26.7) (150)	41 (27.7) (148)	52 (34.7) (150)	52 (34.0) (153)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Lean or Normal in 1982			
Initial Dioxin	n in 1997	Number (%) Obese in 1997	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	133	32 (24.1)	0.83 (0.67,1.02)	0.069
Medium	130	34 (26.2)		
High	122	23 (18.9)		

[a] Adjusted for age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who were lean or had normal body fat in 1982 (see Chapter 7, Statistical Methods).

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY					
	Number (%) Obese/(n) Examination				
Dioxin Category	1982	1985	1987	1992	1997
Comparison	130 (13.7) (948)	181 (19.4) (933)	198 (21.4) (925)	247 (26.6) (929)	282 (29.8) (948)
Background RH	28 (8.1) (347)	35 (10.3) (339)	39 (11.8) (331)	53 (15.7) (337)	66 (19.0) (347)
Low RH	35 (15.2) (230)	49 (21.9) (224)	53 (23.4) (227)	66 (29.6) (223)	79 (34.4) (230)
High RH	44 (18.8) (234)	63 (27.3) (231)	64 (28.1) (228)	81 (35.2) (230)	81 (34.6) (234)
Low plus High RH	79 (17.0) (464)	112 (24.6) (455)	117 (25.7) (455)	147 (32.5) (453)	160 (34.5) (464)

Table 9-14. Longitudinal Analysis of Body Fat (Discrete) (Continued)

Dioxin Category	Lean or Normal in 1982: n in 1997	Lean or Normal in 1982: Number (%) Obese in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	818	166 (20.3)		
Background RH	319	44 (13.8)	0.64 (0.44,0.91)	0.014
Low RH	195	48 (24.6)	1.30 (0.90,1.89)	0.158
High RH	190	41 (21.6)	1.03 (0.70,1.52)	0.876
Low plus High RH	385	89 (23.1)	1.16 (0.87,1.56)	0.316

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who were lean or had normal body fat in 1982 (see Chapter 7, Statistical Methods).

9.2.3.3 Laboratory Variable

9.2.3.3.1 Erythrocyte Sedimentation Rate (Continuous)

The change in erythrocyte sedimentation rate between 1982 and 1997 was examined for associations with group status and dioxin. The change in erythrocyte sedimentation rate between 1982 and 1997 for Ranch Hands in the high dioxin category was significantly greater than for Comparisons during this same time period (Table 9-15(c): p=0.050). All other contrasts involving categorized dioxin (Model 3) and group and initial dioxin (Models 1 and 2, respectively) were nonsignificant (Table 9-15: p>0.13 for all analyses).

Table 9-15. Longitudinal Analysis of Erythrocyte Sedimentation Rate (mm/hr) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS									
		Mean[a]/(n) Examination							
Occupational Category	Group	1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	***Ranch Hand***	***1.83***	***481***	***5.06***	***8.03***	***4.87***	***3.05***	***0.04***	***0.813***
		(819)	***(801)***	***(792)***	***(797)***	***(819)***			
	Comparison	***1.59***	***4.67***	***4.86***	***7.57***	***4.59***	***3.01***		
		(976)	***(958)***	***(949)***	***(956)***	***(976)***			
Officer	Ranch Hand	1.83	4.71	4.81	7.39	4.44	2.61	–0.34	0.213
		(312)	(308)	(304)	(307)	(312)			
	Comparison	1.44	4.65	4.72	7.39	4.38	2.95		
		(380)	(374)	(368)	(375)	(380)			
Enlisted Flyer	Ranch Hand	2.13	5.30	6.04	8.94	5.38	3.25	0.08	0.878
		(148)	(145)	(143)	(145)	(148)			
	Comparison	2.11	5.02	5.02	8.44	5.28	3.17		
		(145)	(144)	(143)	(143)	(145)			
Enlisted Groundcrew	Ranch Hand	1.71	4.71	4.92	8.25	5.07	3.36	0.37	0.138
		(359)	(348)	(345)	(345)	(359)			
	Comparison	1.58	4.58	4.93	7.46	4.57	2.99		
		(451)	(440)	(438)	(438)	(451)			

[a] Transformed from natural logarithm scale of erythrocyte sedimentation rate + 0.1.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of natural logarithm of erythrocyte sedimentation rate + 0.1; results adjusted for natural logarithm of erythrocyte sedimentation rate + 0.1 in 1982 and age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

Table 9-15. Longitudinal Analysis of Erythrocyte Sedimentation Rate (mm/hr) (Continuous) (Continued)

(b) MODEL 2: RANCH HANDS – INITIAL DIOXIN							
Initial Dioxin Category Summary Statistics						Analysis Results for Log₂ (Initial Dioxin)[b]	
	Mean[a]/(n) Examination						
Initial Dioxin	1982	1985	1987	1992	1997	Adjusted Slope (Std. Error)	p-Value
Low	1.71 (154)	4.82 (151)	4.99 (153)	7.94 (149)	4.74 (154)	0.045 (0.031)	0.146
Medium	2.25 (159)	5.52 (156)	5.71 (156)	9.62 (156)	5.94 (159)		
High	1.76 (153)	4.94 (150)	5.53 (148)	8.42 (150)	5.10 (153)		

[a] Transformed from natural logarithm scale of erythrocyte sedimentation rate + 0.1.

[b] Results based on difference between natural logarithm of 1997 erythrocyte sedimentation rate + 0.1 and natural logarithm of 1982 erythrocyte sedimentation rate + 0.1 versus $\log_2$ (initial dioxin); results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of 1982 erythrocyte sedimentation rate + 0.1, and age in 1997.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

Table 9-15. Longitudinal Analysis of Erythrocyte Sedimentation Rate (mm/hr) (Continuous) (Continued)

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY								
Dioxin Category	**Mean[a]/(n) Examination**					**Exam. Mean Change[b]**	**Difference of Exam. Mean Change**	**p-Value[c]**
	1982	**1985**	**1987**	**1992**	**1997**			
Comparison	1.60 (948)	4.66 (933)	4.85 (923)	7.55 (929)	4.60 (948)	3.00		
Background RH	1.72 (347)	4.45 (339)	4.63 (330)	7.27 (337)	4.39 (347)	2.67	–0.33	0.220
Low RH	1.92 (230)	5.06 (224)	5.24 (227)	8.59 (223)	5.12 (230)	3.20	0.20	0.784
High RH	1.87 (236)	5.11 (233)	5.56 (230)	8.70 (232)	5.37 (236)	3.50	0.50	0.050
Low plus High RH	1.89 (466)	5.09 (457)	5.40 (457)	8.65 (455)	5.25 (466)	3.35	0.35	0.143

[a] Transformed from natural logarithm scale of erythrocyte sedimentation rate + 0.1.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of natural logarithm of 1997 erythrocyte sedimentation rate + 0.1; results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of 1982 erythrocyte sedimentation rate + 0.1, and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

9.2.3.3.2 Erythrocyte Sedimentation Rate (Discrete)

Longitudinal analyses of erythrocyte sedimentation rate in its discrete form were conducted to examine the relation between abnormal erythrocyte sedimentation rates and group, initial dioxin, and categorized dioxin for participants at the 1997 follow-up. Only participants with normal erythrocyte sedimentation rates in 1982 were included in the study.

Analyses were statistically significant when erythrocyte sedimentation rate differences were examined across all occupations (Table 9-16(a): Adj. RR=1.66, p=0.016). The results revealed that the percentage of abnormal erythrocyte sedimentation rates for Ranch Hands was higher than for Comparisons (7.0% and 4.4%, respectively). Erythrocyte sedimentation rates compared within the officer strata did not significantly differ (p=0.847). Within the enlisted flyer stratum, the Ranch Hands versus Comparison contrast was marginally significant (Adj. RR=2.61, p=0.077). More Ranch Hand (9.0%) than

Comparison (3.7%) enlisted flyers had abnormal erythrocyte sedimentation rates. In addition, results were significant (Adj. RR=2.03, p=0.025) for the enlisted groundcrew stratum. Percentages of abnormal erythrocyte sedimentation rates were 7.7 for Ranch Hand and 4.2 for Comparison enlisted groundcrew.

A significant positive association between initial dioxin and erythrocyte sedimentation rate was found (Table 9-16(b): Adj. RR=1.36, p=0.022). The analyses indicated that erythrocyte sedimentation rate increased as initial dioxin level increased.

Analyses of associations between erythrocyte sedimentation rates and categorized dioxin revealed significant differences between Comparisons and Ranch Hands in the high and Ranch Hands in the low and high dioxin categories combined (Table 9-16(c): Adj. RR=2.38, p=0.003 and Adj. RR=1.88, p=0.010, respectively). Both contrasts indicate that more Ranch Hands than Comparison had a higher percentage of abnormal erythrocyte sedimentation rates (8.7% for Ranch Hands in the high dioxin category, 7.7% for Ranch Hands in the low and high dioxin categories combined, and 4.3% for Comparisons). The contrasts involving the background and low Ranch Hand dioxin categories were both nonsignificant (p>0.22 for each contrast).

Table 9-16. Longitudinal Analysis of Erythrocyte Sedimentation Rate (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) Abnormal/(n) Examination 1982	1985	1987	1992	1997
All	***Ranch Hand***	***19 (2.3) (819)***	***50 (6.2) (801)***	***54 (6.8) (792)***	***130 (16.3) (797)***	***67 (8.2) (819)***
	Comparison	***39 (4.0) (976)***	***50 (5.2) (958)***	***45 (4.7) (949)***	***153 (16.0) (956)***	***57 (5.8) (976)***
Officer	Ranch Hand	6 (1.9) (312)	10 (3.3) (308)	12 (4.0) (304)	38 (12.4) (307)	18 (5.8) (312)
	Comparison	12 (3.2) (380)	15 (4.0) (374)	14 (3.8) (368)	49 (13.1) (375)	26 (6.8) (380)
Enlisted Flyer	Ranch Hand	4 (2.7) (148)	13 (9.0) (145)	15 (10.5) (143)	30 (20.7) (145)	16 (10.8) (148)
	Comparison	9 (6.2) (145)	10 (6.9) (144)	5 (3.5) (143)	27 (18.9) (143)	5 (3.5) (145)
Enlisted Groundcrew	Ranch Hand	9 (2.5) (359)	27 (7.8) (348)	27 (7.8) (345)	62 (18.0) (345)	33 (9.2) (359)
	Comparison	18 (4.0) (451)	25 (5.7) (440)	26 (5.9) (438)	77 (17.6) (438)	26 (5.8) (451)

Table 9-16. Longitudinal Analysis of Erythrocyte Sedimentation Rate (Discrete) (Continued)

Occupational Category	Group	Normal in 1982: n in 1997	Normal in 1982: Number (%) Abnormal in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***800***	***56 (7.0)***	***1.66 (1.09,2.52)***	***0.016***
	Comparison	***937***	***41 (4.4)***		
Officer	Ranch Hand	306	16 (5.2)	1.07 (0.53,2.14)	0.847
	Comparison	368	18 (4.9)		
Enlisted Flyer	Ranch Hand	144	13 (9.0)	2.61 (0.90,7.55)	0.077
	Comparison	136	5 (3.7)		
Enlisted Groundcrew	Ranch Hand	350	27 (7.7)	2.03 (1.09,3.77)	0.025
	Comparison	433	18 (4.2)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal erythrocyte sedimentation rate (≤12 mm/hr) in 1982 (see Chapter 7, Statistical Methods).

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN

Initial Dioxin	Number (%) Abnormal/(n) Examination: 1982	1985	1987	1992	1997
Low	5 (3.3)	13 (8.6)	7 (4.6)	27 (18.1)	11 (7.1)
	(154)	(151)	(153)	(149)	(154)
Medium	3 (1.9)	14 (9.0)	16 (10.3)	33 (21.2)	18 (11.3)
	(159)	(156)	(156)	(156)	(159)
High	4 (2.6)	13 (8.7)	14 (9.5)	26 (17.3)	15 (9.8)
	(153)	(150)	(148)	(150)	(153)

Table 9-16. Longitudinal Analysis of Erythrocyte Sedimentation Rate (Discrete) (Continued)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1982			
Initial Dioxin	n in 1997	Number (%) Abnormal in 1997	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	149	8 (5.4)	1.36 (1.05,1.76)	0.022
Medium	156	15 (9.6)		
High	149	12 (8.1)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal erythrocyte sedimentation rate (≤ 12 mm/hr) in 1982 (see Chapter 7, Statistical Methods).

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY					
	Number (%) Abnormal/(n) Examination				
Dioxin Category	1982	1985	1987	1992	1997
Comparison	39 (4.1) (948)	50 (5.4) (933)	42 (4.6) (923)	148 (15.9) (929)	55 (5.8) (948)
Background RH	7 (2.0) (347)	10 (3.0) (339)	17 (5.2) (330)	42 (12.5) (337)	22 (6.3) (347)
Low RH	7 (3.0) (230)	19 (8.5) (224)	14 (6.2) (227)	43 (19.3) (223)	20 (8.7) (230)
High RH	5 (2.1) (236)	21 (9.0) (233)	23 (10.0) (230)	43 (18.5) (232)	24 (10.2) (236)
Low plus High RH	12 (2.6) (466)	40 (8.8) (457)	37 (8.1) (457)	86 (18.9) (455)	44 (9.4) (466)

Table 9-16. Longitudinal Analysis of Erythrocyte Sedimentation Rate (Discrete) (Continued)

Dioxin Category	Normal in 1982: n in 1997	Normal in 1982: Number (%) Abnormal in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	909	39 (4.3)		
Background RH	340	20 (5.9)	1.40 (0.80,2.45)	0.238
Low RH	223	15 (6.7)	1.47 (0.79,2.73)	0.225
High RH	231	20 (8.7)	2.38 (1.34,4.23)	0.003
Low plus High RH	454	35 (7.7)	1.88 (1.16,3.03)	0.010

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal erythrocyte sedimentation rate (≤ 12 mm/hr) in 1982 (see Chapter 7, Statistical Methods).

9.3 DISCUSSION

In clinical medicine, the assessment of an individual's general state of health is based on subjective and objective indices including the individual's history, physical examination, and laboratory testing. The variables analyzed in this chapter are frequently employed by clinicians in outpatient practice and were selected to be sensitive to the overall state of health rather than specific to any organ system.

The clinical evaluation of the patient begins with the medical history, which often begins with an intentionally open inquiry into the patient's self-perception of health. In the current examinations, as in most of the previous, a significantly higher percentage of Ranch Hand participants than Comparisons perceived themselves to be in poor health (14.3 percent versus 10.4 percent). Once again the contrast was most apparent in enlisted groundcrew, who had the highest average level of dioxin exposure (18.0 percent of Ranch Hands versus 12.8 percent of Comparisons). In a dose-response pattern, an increasing body burden of dioxin was significantly associated (p=0.002) with negative self-perceptions of health in Ranch Hands in the low, medium, and high 1987 dioxin categories (8.0 percent, 14.3 percent, and 19.3 percent, respectively); this association became marginally significant (p=0.079) with adjustment for relevant covariates. No group differences were noted in the appearance of illness or relative age, as recorded by examining physicians, nor were these variables correlated with serum dioxin levels in the Ranch Hand cohort.

The body fat measure is an easily derived index and, to the extent that it can reflect significant weight gain or loss over time, it can serve as a valuable clinical clue to the presence of occult disease. The prevalence of obesity (>25 percent body fat) was similar in the Ranch Hand and Comparison cohorts. In Ranch Hands by both continuous and discrete analyses, a consistent and highly significant ($p<0.001$ for both) positive association was noted between obesity and the 1987 serum dioxin level. Although a mobile equilibrium exists between serum dioxin and adipose tissue, the current results confirm those of the 1992 examinations and suggest a difference in dioxin pharmacokinetics in obese versus lean individuals.

The erythrocyte sedimentation rate can be a sensitive, if nonspecific, index of general health. The effect of age on the erythrocyte sedimentation rate is pertinent to the longitudinal design of the current study: a rate as high as 40 millimeters per hour is not considered unusual at age 65. Extreme elevations in the erythrocyte sedimentation rate consistently are associated with serious underlying infections, inflammation, or malignant disease processes.

In prior examinations, erythrocyte sedimentation rate analyses have yielded inconsistent results. In the 1985 and 1987 examinations (but not in 1982 or 1992), abnormally elevated erythrocyte sedimentation rates were significantly more prevalent in Ranch Hands than Comparisons. In the 1987 and 1992 examinations, dioxin analyses raised the possibility of a subtle dose-response inflammatory effect occurring in association with initial and then current serum dioxin levels. In the 1992 examinations, for example, the Ranch Hand enlisted groundcrew, the occupation with the highest average dioxin level, had a slightly higher mean erythrocyte sedimentation rate than Comparisons, but the difference (9.27 mm/hr versus 8.43 mm/hr) cannot be considered clinically meaningful. In the models that employed 1987 serum dioxin levels, the analyses yielded results that were consistent with a subtle dose-response effect, but the differences were slight and of uncertain biologic meaning.

Similarly, in this current study, by both continuous and discrete analyses, significant associations were noted between the erythrocyte sedimentation rate and 1987 serum dioxin levels. In a pattern consistent with a dose-response effect, Ranch Hand participants in the low, medium, and high 1987 dioxin categories had abnormally elevated erythrocyte sedimentation rates of 6.6, 8.0, and 9.7 percent, respectively. By continuous analysis, the differences in the means were so slight (adjusted means of 4.34 mm/hr, 4.62 mm/hr, and 5.29 mm/hr in the low, medium, and high 1987 dioxin categories, respectively) as to be of doubtful clinical meaning. As in the 1992 examinations, the erythrocyte sedimentation rate analyses found no group differences between the Ranch Hand and Comparison cohorts.

Dependent variable-covariate analyses confirm numerous associations that have been documented in previous AFHS examinations and that are well-established in clinical practice. Consequent to the higher incidence of nicotine-related cardiovascular and pulmonary disease that occurs by middle age, cigarette smokers often appear older and more chronically ill than nonsmokers and perceive themselves as such. That the highest prevalence of obesity (33.6 percent) was found in reformed smokers is consistent with the weight gain that so often occurs with smoking cessation. Given the high incidence of chronic bronchitis associated with cigarette use, it is not surprising that the highest prevalence of abnormally elevated erythrocyte sedimentation rates (12.4 percent) was noted in those smoking more than one pack per day.

Analyses based on associations with occupation confirm previous AFHS results. As a group, officers continue to appear healthier than enlisted personnel by several indices including perceptions of health, relative age appearance, and body fat. Older participants were more likely to have abnormally elevated erythrocyte sedimentation rates than younger participants.

Longitudinal analyses confirm results and trends that have been established over 15 years of observation. At the baseline examination in 1982, the prevalence of self-perceived ill health was significantly greater in Ranch Hands than Comparisons (18.7 percent versus 13.2 percent). By 1987, despite advancing age, the percentage of Ranch Hands and Comparisons reporting ill health declined to 5.5 percent and 4.4 percent, respectively. In 1992 this trend was reversed, particularly in those Ranch Hands in the medium and high categories of current and initial levels of serum dioxin. In the 1997 examinations there has been a close to identical increase (40 percent) in the prevalence of reported poor health in each cohort (14.4 percent versus 10.6 percent), a trend that is consistent with the increased incidence of chronic illness in any aging population and that is now independent of all indices of exposure to dioxin. In contrast, in neither the appearance of illness or distress nor in relative age appearance were there any significant associations with the 1987 body burden of dioxin.

In the 1985 and 1987 examinations, Ranch Hand participants were noted to have a higher percentage of abnormal erythrocyte sedimentation rates than Comparisons and, in 1987, a significant positive association was found between group and the change in the percentage of abnormal erythrocyte sedimentation rates. In 1992, the prevalence of abnormal erythrocyte sedimentation rates was close to identical in the two cohorts with no evidence of a dioxin effect. In the current study, Ranch Hands once again have a significantly higher percentage of abnormal erythrocyte sedimentation rates than Comparisons (7.0 percent versus 4.4 percent of participants considered normal in 1982) in a pattern consistent with a dose response. This pattern also was present with categorized dioxin, where 8.7 percent of Ranch Hands with the highest levels of serum dioxin had an abnormally elevated erythrocyte sedimentation rate, compared with 4.3 percent of Comparisons ($p=0.003$). This positive association raises the possibility of a subtle inflammatory, infectious, or occult malignant disease process related to the body burden of dioxin.

In summary, consistent with all previous examinations, Ranch Hands continue to perceive themselves as less healthy than Comparisons. Since the last examinations in 1992, a comparable and significant increase in the prevalence of self-perceived ill health has occurred in both cohorts and is consistent with the inevitable development of chronic disease in any aging population.

9.4 SUMMARY

9.4.1 Model 1: Group Analysis

The unadjusted and adjusted group analyses (Ranch Hands versus Comparisons) produced similar results for each variable examined within the general health assessment. The self-perception of health analysis revealed significant differences among Ranch Hands and Comparisons across all occupations and within the enlisted groundcrew stratum. For both contrasts, more Ranch Hands than Comparisons indicated their health as fair or poor. All other group analyses were nonsignificant. The results are summarized in Table 9-17.

Longitudinal analyses of erythrocyte sedimentation rate in its discrete form indicated that significantly more Ranch Hands then Comparisons were normal in 1982 and abnormal in 1997. This difference was noted in the two enlisted strata.

Table 9-17. Summary of Group Analysis (Model 1) for General Health Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Questionnaire				
Self-perception of Health (D)	+0.007	NS	NS	+0.028
Physical Examination				
Appearance of Illness or Distress (D)	NS	NS	NS	NS
Relative Age Appearance (D)	NS	NS	NS	NS
Body Fat (C)	ns	ns	ns	ns
Body Fat (D)	ns	NS	ns	ns
Laboratory				
Erythrocyte Sedimentation Rate (C)	NS	ns	ns	NS
Erythrocyte Sedimentation Rate (D)	NS	ns	NS	NS

Note: NS or ns: Not significant (p>0.10).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Variable	ADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Questionnaire				
Self-perception of Health (D)	+0.010	NS	NS	+0.035
Physical Examination				
Appearance of Illness or Distress (D)	NS	NS	NS	NS
Relative Age Appearance (D)	NS	NS	NS	NS
Body Fat (C)	ns	ns	ns	ns
Body Fat (D)	ns	NS	ns	ns
Laboratory				
Erythrocyte Sedimentation Rate (C)	NS	ns	ns	NS
Erythrocyte Sedimentation Rate (D)	NS	ns	NS	NS

Note: NS or ns: Not significant (p>0.10).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00.

P-value given if p≤0.05.

Table 9-17. Summary of Group Analysis (Model 1) for General Health Variables (Ranch Hands vs. Comparisons) (Continued)

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

9.4.2 Model 2: Initial Dioxin Analysis

The unadjusted analysis of body fat in its continuous form revealed a marginally significant association between body fat and initial dioxin. The relative risk estimate for the adjusted analysis became significant, with body fat increasing as initial dioxin increased. All remaining analyses of other variables examined revealed nonsignificant results, as shown in Table 9-18.

A significant relation was observed in longitudinal analyses between abnormal erythrocyte sedimentation rates in 1997 and initial dioxin for participants who had normal erythrocyte sedimentation rates in 1982. The percentage of participants who were normal in 1982 and abnormal in 1997 increased as initial dioxin increased.

Table 9-18. Summary of Initial Dioxin Analysis (Model 2) for General Health Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Questionnaire		
Self-perception of Health (D)	NS	ns
Physical Examination		
Appearance of Illness or Distress (D)	ns	ns
Relative Age Appearance (D)	NS	NS
Body Fat (C)	NS*	+0.020
Body Fat (D)	NS	NS
Laboratory		
Erythrocyte Sedimentation Rate (C)	NS	NS
Erythrocyte Sedimentation Rate (D)	NS	NS

Note: NS or ns: Not significant ($p>0.10$).
NS*: Marginally significant ($0.05<p\leq0.10$).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk $\geq$ 1.00.

P-value given if $p\leq0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

9.4.3 Model 3: Categorized Dioxin Analysis

Table 9-19 summarizes the results of the categorized dioxin analyses. More Ranch Hands in the low dioxin category and in the low and high combined Ranch Hand category appeared ill or distressed than did Comparisons, without adjustment for covariates. After adjustment for covariates, the result was marginally significant in the low dioxin category and nonsignificant in the low and high combined Ranch Hand category contrasts.

The unadjusted and adjusted analyses of categorized dioxin yielded similar results for the self-perception of health and body fat (continuous) variables. Significantly more Ranch Hands than Comparisons perceived their health to be fair or poor when the low, high, and low and high combined Ranch Hand dioxin categories were contrasted with Comparisons. For the continuous analyses of body fat, the mean in the background Ranch Hand category was significantly lower than the Comparison mean, and the means in the low, high, and low and high combined Ranch Hand dioxin categories were significantly or marginally significantly higher than the Comparison mean.

Unadjusted and adjusted analyses of body fat in its discrete form revealed a significantly lower percentage of obese Ranch Hands in the background dioxin category, and a marginally significant higher percentage of obese Ranch Hands in the low dioxin category, than Comparisons. In the combined low and high dioxin category, a significantly greater percentage of Ranch Hands than Comparisons were obese; this difference was marginally significant after adjustment for covariates.

All results for categorized dioxin analysis of relative age appearance and the discrete and continuous forms of erythrocyte sedimentation rate were nonsignificant.

Longitudinal analyses revealed significantly more Ranch Hands in the low dioxin category than Comparisons who were normal in 1982, but appeared ill or distressed in 1987. The difference between Ranch Hands in the high dioxin category and Comparisons was not significant.

The percentage of participants with abnormal erythrocyte sedimentation rates in 1997, who were normal in 1982, increased as categorized dioxin increased. Ranch Hands in the high dioxin category had a significantly greater percentage of 1997 erythrocyte sedimentation rate abnormalities than Comparisons, based on both cohorts being normal in 1982.

Table 9-19. Summary of Categorized Dioxin Analysis (Model 3) for General Health Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Questionnaire				
Self-perception of Health (D)	ns	+0.005	+<0.001	+<0.001
Physical Examination				
Appearance of Illness or Distress (D)	ns	+0.031	NS	+0.041
Relative Age Appearance (D)	NS	NS	NS	NS
Body Fat (C)	–<0.001	+0.045	0.001	<0.001
Body Fat (D)	–<0.001	NS*	ns	+0.042
Laboratory				
Erythrocyte Sedimentation Rate (C)	ns	NS	NS	NS
Erythrocyte Sedimentation Rate (D)	NS	NS	NS	NS

Note: NS or ns: Not significant ($p>0.10$).
NS*: Marginally significant ($0.05<p\leq 0.10$).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00 for discrete analysis; difference of means nonnegative for continuous analysis.
–: Difference of means negative for continuous analysis.

P-value given if $p\leq 0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 9-19. Summary of Categorized Dioxin Analysis (Model 3) for General Health Variables (Ranch Hands vs. Comparisons) (Continued)

	ADJUSTED			
Variable	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Questionnaire				
Self-perception of Health (D)	NS	+0.020	+0.002	+0.001
Physical Examination				
Appearance of Illness or Distress (D)	ns	NS*	NS	NS
Relative Age Appearance (D)	NS	NS	NS	NS
Body Fat (C)	–<0.001	NS*	0.001	0.001
Body Fat (D)	–0.001	NS*	NS	NS*
Laboratory				
Erythrocyte Sedimentation Rate (C)	ns	NS	NS	NS
Erythrocyte Sedimentation Rate (D)	NS	NS	NS	NS

Note: NS or ns: Not significant ($p>0.10$).
NS*: Marginally significant ($0.05<p\leq0.10$).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00 for discrete analysis.
–: Relative risk < 1.00 for discrete analysis; difference of means negative for continuous analysis.

P-value given if $p\leq0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

9.4.4 Model 4: 1987 Dioxin Level Analysis

Several significant associations between the measures of general health studied in this assessment and the 1987 dioxin level associations were found, as presented in Table 9-20. Each of the unadjusted analyses of associations of 1987 dioxin levels and self-perception of health, body fat (continuous and discrete forms), and erythrocyte sedimentation rate (continuous and discrete forms) were significant. For these significant associations, discrete analyses produced relative risks greater than 1.0, and continuous analyses showed an increase in body fat and erythrocyte sedimentation rate as 1987 dioxin levels increased. After covariate adjustments, results remained significant for the body fat (continuous and discrete) adjusted analyses. The adjusted analysis of erythrocyte sedimentation rate in its continuous form also remained significant in the adjusted analysis, but the result was nonsignificant for the discrete adjusted analysis. The association between 1987 dioxin levels and self-perception of health became marginally significant. Associations were nonsignificant for both unadjusted and adjusted analyses of appearance of illness or distress and relative age appearance.

Table 9-20. Summary of 1987 Dioxin Analysis (Model 4) for General Health Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Questionnaire		
Self-perception of Health (D)	+0.002	NS*
Physical Examination		
Appearance of Illness or Distress (D)	NS	NS
Relative Age Appearance (D)	ns	ns
Body Fat (C)	+<0.001	+<0.001
Body Fat (D)	+<0.001	+<0.001
Laboratory		
Erythrocyte Sedimentation Rate (C)	+0.004	+0.037
Erythrocyte Sedimentation Rate (D)	+0.040	NS

Note: NS or ns: Not significant ($p>0.10$).
NS*: Marginally significant ($0.05<p\leq0.10$).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00 for discrete analysis; slope nonnegative for continuous analysis.

P-value given if $p\leq0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

9.5 CONCLUSION

The self-perception of health analysis revealed significant differences among Ranch Hands and Comparisons, with more Ranch Hands than Comparisons indicating their health as fair or poor. As in previous examinations, the difference was most apparent in enlisted groundcrew, who had the highest average dioxin levels. This observation also was confirmed in the categorized dioxin analysis, where Ranch Hands with the highest dioxin levels perceived their health as fair or poor more often than Comparisons. Also, among Ranch Hands, those with the higher 1987 dioxin levels reported fair or poor health more often than Ranch Hands with lower levels. These results are consistent with the 1985, 1987, and 1992 examinations. No group differences were noted in the appearance of illness or relative age, as recorded by examining physicians, nor were these variables correlated with serum dioxin levels in the Ranch Hand cohort.

The analysis of body fat indicated positive associations with dioxin levels. The results of the 1997 examination confirmed those of the 1992 examination and appear consistent with a difference in dioxin pharmacokinetics in obese versus lean individuals.

No differences in the percentages of abnormal erythrocyte sedimentation rates between Ranch Hands and Comparisons or relations between abnormal erythrocyte sedimentation rates and dioxin levels were observed during the 1997 examination. Erythrocyte sedimentation rates increased as 1987 dioxin levels increased.

Longitudinal analyses showed that Ranch Hands, particularly the two enlisted strata, had an increased percentage of abnormal erythrocyte sedimentation rates than did Comparisons over the 15 years of the study since 1982. These analyses also showed that the percentages of abnormalities increased from 1982 to 1997 as dioxin levels increased. This result was seen at the 1987 study, but not in 1992. This positive association raises the possibility of a subtle inflammatory, infectious, or occult malignant disease process related to the body burden of dioxin.

In conclusion, fair or poor self-perception of health displayed an adverse association with dioxin, but the relation with other health conditions is unknown. Increased body fat was associated with increased levels of dioxin exposure, a finding most likely related to the pharmacokinetics of dioxin elimination. Longitudinal analyses indicate an increased percentage of abnormal erythrocyte sedimentation rates in Ranch Hands over Comparisons in the 15 years of the AFHS, and a relation between abnormal erythrocyte sedimentation rates and levels of dioxin during these 15 years. Other measures of general health revealed no association with levels of dioxin.

REFERENCES

1. Institute of Medicine. 1994. *Veterans and Agent Orange: Health Effects of Herbicides Used in Vietnam.* National Academy Press: Washington, DC.
2. Institute of Medicine. 1996. *Veterans and Agent Orange: Update 1996.* National Academy Press: Washington, DC.
3. Kancir, C. B., C. Andersen, and A. S. Olesen. 1988. Marked hypocalcemia in a fatal poisoning with chlorinated phenoxy acid derivatives. *Clinical Toxicology* 26:257-64.
4. Flanagan, R. J., T. J. Meredith, M. Ruprah, L. J. Onhon, and A. Liddle. 1990. Alkaline diuresis for acute poisoning with chlorophenoxy herbicides and ioxynil. *Lancet* 335:454-8.
5. Lathrop, G. D., W. H. Wolfe, R. A. Albanese, and P. M. Moynahan. 1984. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Baseline Morbidity Study Results. NTIS: AD A-138-340. United States Air Force School of Aerospace Medicine, Brooks Air Force Base, Texas.
6. Lathrop, G. D., S. G. Machado, T. G. Karrison, W. D. Grubbs, W. F. Thomas, W. H. Wolfe, J. E. Michalek, J. C. Miner, and M. R. Peterson. 1987. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: First followup examination results. NTIS: AD A 188262. United States Air Force School of Aerospace Medicine, Brooks Air Force Base, Texas.
7. Thomas, W. F., W. D. Grubbs, T. G. Karrison, M. B. Lustik, R. H. Roegner, D. E. Williams, W. H. Wolfe, J. E. Michalek, J. C. Miner, and R. W. Ogershok. 1990. An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: I. 1987 followup examination results, May 1987 to January 1990. NTIS: AD A 222 573. United States Air Force School of Aerospace Medicine, Human Systems Division (AFSC), Brooks Air Force Base, Texas.
8. Roegner, R. H., W. D. Grubbs, M. B. Lustik, A. S. Brockman, S. C. Henderson, D. E. Williams, W. H. Wolfe, J. E. Michalek, and J. C. Miner. 1991. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides. Serum dioxin analysis of 1987 examination results. NTIS: AD A 237 516-24. United States Air Force School of Aerospace Medicine, Brooks Air Force Base, Texas.
9. Grubbs, W. D., W. H. Wolfe, J. E. Michalek, D. E. Williams, M. B. Lustik, A. S. Brockman, S. C. Henderson, F. R. Burnett, R. G. Land, D. J. Osborne, V. K. Rocconi, M. E. Schreiber, J. C. Miner, G. L. Henriksen, and J. A. Swaby. 1995. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final Report. 1992 Followup Examination Results. NTIS: AD A 304 306, 304 308-316. United States Air Force School of Aerospace Medicine, Brooks Air Force Base, Texas.
10. Visintainer, P. F., M. Barone, H. McGee, and E. L. Peterson. 1995. Proportionate mortality study of Vietnam-era veterans of Michigan. *Journal of Occupational and Environmental Medicine* 37:423-8.
11. Centers for Disease Control. 1989. Health status of Vietnam veterans. Vietnam Experience Study. Atlanta: U.S. Department of Health and Human Services. Vols. I-V, Supplements A-C.

12. Centers for Disease Control. 1990. The Association of Selected Cancers with Service in the U.S. Military in Vietnam: Final Report, Atlanta: U.S. Department of Health and Human Services.

13. Dalager, N. A., H. K. Kang, and T. L. Thomas. 1995. Cancer mortality patterns among women who served in the military: the Vietnam experience. *Journal of Occupational and Environmental Medicine* 37:298-305.

14. Bullman, T. A., K. K. Watanabe, and H. K. Kang. 1994. Risk of testicular cancer associated with surrogate measures of Agent Orange exposure among Vietnam veterans of the Agent Orange Registry. *Annals of Epidemiology* 4:11-6.

15. Wolfe, W. H., J. E. Michalek, J. C. Miner, A. Rahe, J. Silva, W. F. Thomas, W. D. Grubbs, M. B. Lustik, T. G. Karrison, R. H. Roegner, and D. E. Williams. 1990. Health status of Air Force veterans occupationally exposed to herbicides in Vietnam. I. Physical health. *Journal of the American Medical Association* 264:1824-31.

16. Fingerhut, M. A., W. E. Halperin, D. A. Marlow, L. A. Piacitelli, P. A. Honchar, M. H. Sweeney, A. L. Greife, P. A. Dill, K. Steenland, and A. J. Suruda. 1991. Cancer mortality in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *New England Journal of Medicine* 324:212-8.

17. Asp, S., V. Riihimaki, S. Hernberg, and E. Pukkala. 1994. Mortality and cancer morbidity of Finnish chlorophenoxy herbicide applicators: an 18-year prospective followup. *American Journal of Industrial Medicine* 26:243-53.

18. Bueno de Mesquita, H. B., G. Doornbos, D. A. Van der Kuip, M. Kogevinas, and R. Winkelmann. 1993. Occupational exposure to phenoxy herbicides and chlorophenols and cancer mortality in the Netherlands. *American Journal of Industrial Medicine* 23:289-300.

19. Saracci, R., M. Kogenvinas, P. A. Bertazzi, B. H. Bueno de Mesquita, D. Coggon, L. M. Green, T. Kauppinen, K. A. L'Abbe, M. Littorin, E. Lynge, J. D. Mathews, M. Neuberger, J. Osman, N. Pearce, and R. Winkelmann. 1991. Cancer mortality in workers exposed to chlorophenoxy herbicides and chlorophenols. *Lancet* 38:1027-32.

20. Coggon, D., B. Pannett, and P. Winter. 1991. Mortality and incidence of cancer at four factories making phenoxy herbicides. *British Journal of Industrial Medicine* 48:173-8.

21. Eriksson, M., and L. Hardell. 1991. New experiences strengthen the connection between dioxins, phenoyxy acids and malignant tumors. *Lakartidningen* 88:2210-1.

22. Eriksson, M., L. Hardell, H. Malker, and J. Weiner. 1992. Malignant lymphoproliferative diseases in occupations with potential exposure to phenoxyacetic acid or dioxins: a register-based study. *American Journal of Industrial Medicine* 22:305-12.

23. Manz, A., J. Berger, J. H. Dwyer, D. Flesch-Janys, S. Nagel, and H. Waltsgott. 1991. Cancer mortality among workers in chemical plant contaminated with dioxin. *Lancet* 338:959-64.

24. Eriksson, M., L. Hardell, and H. O. Adami. 1990. Exposure to dioxins as a risk factor for soft tissue sarcoma: A population-based case-control study. *Journal of the National Cancer Institute* 82:486-90.

25. Kogevinas, M., R. Saracci, P. A. Bertazzi, B. H. Bueno de Mesquita, D. Coggon, L. M. Green, T. Kauppinen, M. Littorin, E. Lynge, J. D. Mathews, M. Neuberger, J. Osman, N. Pearce, and R. Winkelmann. 1992. Cancer mortality from soft-tissue sarcoma and malignant lymphomas in an international cohort of workers exposed to chlorophenoxy herbicides and chlorophenols. *Chemosphere* 25:1071-6.

26. Kogevinas, M., T. Kauppinen, R. Winkelmann, H. Becher, P. A. Bertazzi, B. Bas, D. Coggon, D. Green, E. Johnson, M. Littorin, E. Lynge, D. A. Marlow, J. D. Mathews, M. Neuberger, T. Benn, B. Pannett, N. Pearce, and R. Saracci. 1995. Soft tissue sarcoma and non-Hodgkin's lymphoma in workers exposed to phenoxy herbicides, chlorophenols and dioxins: two nested case-control studies. *Epidemiology* 6:396-402.

27. Hardell, L., M. Eriksson, and A. Degerman. 1994. Exposure to phenoxyacetic acids, chlorophenols, or organic solvents in relation to histopathology, stage, and anatomical localization of non-Hodgkin's lymphoma. *Cancer Research* 54:2386-9.

28. Calvert, G. M., M. H. Sweeney, M. A. Fingerhut, R. W. Hornung, and W. E. Halperin. 1994. Evaluation of porphyria cutanea tarda in U.S. workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *American Journal of Industrial Medicine* 25:559-71.

29. Collins, J. J., M. E. Strauss, G. J. Levinskas, and P. R. Conner. 1993. The mortality experience of workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin in a trichlorophenol-process accident. *Epidemiology* 4:7-13.

30. Assennato, G., D. Cervino, E. A. Emmett, G. Longo, and F. Merlo. 1989. Followup of subjects who developed chloracne following TCDD exposure at Seveso. *American Journal of Industrial Medicine* 16:119-25.

31. Assennato, G., P. Cannatelli, E. Emmett, I. Ghezzi, and F. Merlo. 1989. Medical monitoring of dioxin clean-up workers. *American Industrial Hygiene Association Journal* 50:586-92.

32. Bertazzi, P. 1991. Long-term effects of chemical disasters. Lessons and results from Seveso. *Science of the Total Environment* 106:5-20.

33. Bertazzi, P. A., A. C. Pesatori, D. Consonni, A. Tironi, M. T. Landi, and C. Zocchetti. 1993. Cancer incidence in a population accidentally exposed to 2,3,7,8-tetrachlorodibenzo-para-dioxin. *Epidemiology* 4:398-406.

34. Mocarelli, P., A. Marocchi, P. Brambilla, P. Gerthoux, L. Colombo, A. Mondonico, and L. Meazza. 1991. Effects of dioxin exposure in humans at Seveso, Italy. Banbury Report 35 (Biological Basis for Risk Assessment of Dioxins and Related Compounds): 95-110.

35. Zober, A., P. Messerer, and P. Huber. 1990. Thirty-four-year mortality followup of BASF employees exposed to 2,3,7,8-TCDD after the 1953 accident. *International Archives of Occupational and Environmental Health* 62:139-57.

36. Zober, M. A., M. G. Ott, O. Papke, K. Senft, and C. Germann. 1992. Morbidity study of extruder personnel with potential exposure to brominated dioxins and furans. I. Results of blood monitoring and immunological tests. *British Journal of Industrial Medicine* 49:532-44.

37. Zober, A., M. G. Ott, and P. Messerer. 1994. Morbidity followup study of BASF employees exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) after a 1953 chemical reactor incident. *Occupational and Environmental Medicine* 51:479-86.

38. Information Ventures, Inc. 1992. Review of literature on herbicides, including phenoxy herbicides and associated dioxins. Vol. XX: Analysis of recent literature on health effects, and Vol. XX: Annotated bibliography of recent literature on health effects. U.S. Veterans Administration, Dept. of Medicine and Surgery, Washington, DC.

39. Information Ventures, Inc. 1993. Review of literature on herbicides, including phenoxy herbicides and associated dioxins. Vol. XXI: Analysis of recent literature on health effects, and Vol. XXII: Annotated bibliography of recent literature on health effects. U.S. Veterans Administration, Dept. of Medicine and Surgery, Washington, DC.

40. Information Ventures, Inc. 1994. Review of literature on herbicides, including phenoxy herbicides and associated dioxins. Vol. XXIII: Analysis of recent literature on health effects, and Vol. XXIV: Annotated bibliography of recent literature on health effects. U.S. Veterans Administration, Dept. of Medicine and Surgery, Washington, DC.

41. Poland, A., and J. C. Knutson. 1982. 2,3,7,8-Tetrachlorodibenzo-p-dioxin and related halogenated aromatic hydrocarbons: Examination of the mechanism of toxicity. *Annual Review of Pharmacology and Toxicology* 22:517-54.

42. Denison, M. S., L. M. Vella, and A. B. Okey. 1986. Structure and function of the Ah receptor for 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Journal of Biological Chemistry* 261:3987-95.

43. Okey, A. B., D. S. Riddick, and P. A. Harper. 1994. The Ah receptor: Mediator of toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and related compounds. *Toxicology Letters* 70:1-22.

44. Denison, M. S. 1992. Heterogeneity of rat hepatic Ah receptor: identification of two receptor forms which differ in their biochemical properties. *Journal of Biochemical Toxicology* 7:249-56.

45. Roa, V. R. 1991. Molecular mechanism of action of dioxin-implications of its carcinogenic potency estimation. *Toxic Substances Journal* 8:335-51.

46. Huff, J., G. Lucier, and A. Tritscher. 1994. Carcinogenicity of TCDD: experimental, mechanistic, and epidemiologic evidence. *Annual Review of Pharmacology and Toxicology* 34:343-72.

47. Neubert, D. 1992. Evaluation of toxicity of TCDD in animals as a basis for human risk assessment. *Toxic Substances Journal* 12:237-76.

48. Birnbaum, L. S. 1993. EPA's reassessment of dioxin risk: directed health research. *Chemosphere* 27:469-75.

49. Dickson, L. C., and S. C. Buzik. 1993. Health risks of "dioxins:" a review of environmental and toxicological considerations. *Veterinary and Human Toxicology* 35:68-77.

50. Houk, V. N. 1992. Review of research on health effects of PCDDs and PCDFs to develop human risk assessment. *Toxic Substances Journal* 12:181-90.

51. Roberts, E. A., K. C. Johnson, P. A. Harper, and A. B. Okey. 1990. Characterization of the Ah receptor mediating aryl hydrocarbon hydroxylase induction in the human liver cell line Hep G2. *Archives of Biochemistry and Biophysics* 276:442-50.

52. Waithe, W., M. Michaud, P. Harper, A. Okey, and A. Anderson. 1991. The Ah receptor, cytochrome P450IA1 mRNA induction, and aryl hydrocarbon hydroxylase in a human lymphoblastoid cell line. *Biochemical Pharmacology* 41:85-92.

53. Lorenzen, A., and A. B. Okey. 1991. Detection and characterization of Ah receptor in tissue and cells from human tonsils. *Toxicology and Applied Pharmacology* 107:203-14.

54. Lucier, G. W. 1991. Humans are sensitive species to some of the biochemical effects of structural analogs of dioxin. *Environmental Toxicology and Chemistry* 10:727-35.

55. Wang, X., M. Santostefano, Y. Lu, and S. Safe. 1992. A comparison of the mouse versus human aryl hydrocarbon (Ah) receptor complex: effects of proteolysis. *Chemico-Biological Interactions* 85:79-93.

56. Wang, X., R. Rosengren, V. Morrison, and S. Safe. 1992. Characterization of the human Ah receptor. *Chemosphere* 25:997-1000.

57. Patterson, D. G., L. Hampton, L. C. R. Lapeza Jr., W. T. Belser, V. Green, L. Alexander, and L. L. Needham. 1987. High resolution gas chromatographic/high-resolution mass spectrometric analysis of human serum on a whole-weight and lipid basis for 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Analytical Chemistry* 59:2000-5.

58. Michalek, J. E., J. L. Pirkle, S. P. Caudill, R. C. Tripathi, D. G. Patterson Jr., and L. L. Needham. 1996. Pharmacokinetics of TCDD in Veterans of Operation Ranch Hand: 10-year Followup. *Journal of Toxicology and Environmental Health* 47:209-20.

59. Needham, L. L., P. M. Gerthoux, D. G. Patterson, P. Brambilla, J. L. Pirkle, P. I. Tramaccre, W. E. Turner, C. Beretta, E. J. Sampson, and P. Mocarelli. 1994. Half-life of 2,3,7,8-tetrachlorodibenzo-p-dioxin in serum of Seveso adults: interim report. *Organohalogen Compounds* 21:81-5.

60. Flesch-Janys, D., P. Gurn, D. Jung, J. Konietzke, and O. Papke. 1994. First results of an investigation of the elimination of polychlorinated dibenzo-p-dioxins and dibenzofurans (PCDD/F) in occupationally exposed persons. *Organohalogen Compounds* 21:93-9.

61. Michalek, J. E., R. C. Tripathi, P. M. Kulkarni, and J. L. Pirkle. 1996. The reliability of the serum dioxin measurement in veterans of Operation Ranch Hand. *Journal of Exposure Analysis and Environmental Epidemiology* 6:327-38.

62. Michalek, J. E., R. Tripathi, S. Caudill, and J. L. Pirkle. 1992. Investigation of TCDD half-life heterogeneity in veterans of Operation Ranch Hand. *Journal of Toxicology and Environmental Health* 35:29-38.

63. U.S. Centers for Disease Control (USCDC). 1988. Serum 2,3,7,8-tetrachlorodibenzo-p-dioxin levels in US Army Vietnam-Era veterans. *Journal of the American Medical Association* 260:1249-54.

64. Kang, H. K., K. K. Watanabe, J. Breen, J. Remmers, M. G. Conomos, J. Stanley, and M. Flicker. 1991. Dioxins and dibenzofurans in adipose tissue of US Vietnam veterans and controls. *American Journal of Public Health* 813:344-9.

65. Michalek, J. E., W. H. Wolfe, J. C. Miner, T. M. Papa, and J. L. Pirkle. 1995. Indices of TCDD exposure and TCDD body burden in Veterans of Operation Ranch Hand. *Journal of Exposure Analysis and Environmental Epidemiology* 5:209-23.

66. Fingerhut, M. A., M. H. Sweeney, D. G. Patterson Jr., L. A. Piacitelli, J. A. Morris, D. A. Marlow, R. W. Hornung, L. W. Cameron, L. B. Connally, L. L. Needham, and W. E. Halperin. 1989. Levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin in the serum of U.S. chemical workers exposed to dioxin contaminated products: Interim results. *Chemosphere* 19:835-40.

67. Schecter, A., H. McGee, J. Stanley, and K. Boggess. 1992. Dioxin, dibenzofuran, and PCB, including coplanar PCB levels in the blood of Vietnam veterans in the Michigan Agent Orange Study. *Chemosphere* 24:205-8.

68. Piacitelli, L. A., M. H. Sweeney, M. A. Fingerhut, D. G. Patterson, W. E. Turner, L. B. Connally, K. K. Wille, and B. Tompkins. 1992. Serum levels of PCDDs and PCDFs among workers exposed to 2,3,7,8-TCDD contaminated chemicals. *Chemosphere* 25:251-4.

69. Pirkle, J., and V. Houk. 1992. Use of epidemiologic studies to assess human risk from exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Chemosphere* 25:1109-16.

70. Sweeney, M. H., M. A. Fingerhut, D. G. Patterson Jr., L. B. Connally, L. A. Piacitelli, J. A. Morris, A. L. Greife, R. W. Hornung, D. A. Marlow, J. E. Dugle, W. E. Halperin, and L. L. Needham. 1990. Comparison of serum levels of 2,3,7,8-TCDD in TCP production workers and in an unexposed comparison group. *Chemosphere* 20:993-1000.

71. Ott, M. G., P. Messerer, and A. Zober. 1993. Assessment of past occupational exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin using blood lipid analyses. *International Archives of Occupational and Environmental Health* 65:1-8.

72. Zober, A., and O. Papke. 1993. Concentrations of PCDDs and PCDFs in human tissue 36 years after accidental dioxin exposure. *Chemosphere* 27:413-8.

73. Flesch-Janys, D., J. Berger, J. Konietzko, A. Manz, S. Nagel, and J. Wahrendorf. 1992. Quantification of exposure to dioxins and furans in a cohort of workers of an herbicide producing plant in Hamburg, FRG. *Chemosphere* 25:1021-8.

74. Schecter, A., J. J. Ryan, O. Papke, M. Ball, and A. Lis. 1993. Elevated dioxin levels in the blood of male and female Russian workers with and without chloracne 25 years after phenoxyherbicide exposure: The UFA "Khimprom" incident. *Chemosphere* 27:253-8.

75. Fedorov, L. A. 1993. Dioxin problem in Russian chemical industry. *Chemosphere* 27:477-81.

76. Smith, A., D. J. Patterson, M. Warner, R. MacKenzie, and L. Needham. 1992. Serum 2,3,7,8-tetrachlorodibenzo-p-dioxin levels of New Zealand pesticide applicators and their implication for cancer hypotheses. *Journal of the National Cancer Institute* 84:104-8.

77. Neuberger, M., W. Landvoigt, and F. Derntl. 1991. Blood levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin in chemical workers after chloracne and in comparison groups. *International Archives of Occupational and Environmental Health* 63:325-8.

78. Johnson, E. W., W. Parsons, C. R. Weinberg, D. L. Shore, J. Mathews, D. G. Patterson, and L. L. Needham. 1992. Current serum levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin in phenoxy acid herbicide applicators and characterization of historical levels. *Journal of the National Cancer Institute* 84:1648-53.

79. Mocarelli, P., L. L. Needham, A. Marocchi, D. G. Patterson Jr., P. Brambilla, P. M. Gerthoux, L. Meazza, and V. Carreri. 1991. Serum concentrations of 2,3,7,8-tetrachlorodibenzo-p-dioxin and test results from selected residents of Seveso, Italy. *Journal of Toxicology and Environmental Health* 32:357-66.

80. Ott, M. G., A. Zober, and C. Germann. 1994. Laboratory results for selected target organs in 138 individuals occupationally exposed to TCDD. *Chemosphere* 29:2423-37.

81. Sweeney, M. H., M. A. Fingerhut, J. C. Arezzo, R. W. Hornung, and L. B. Connally. 1993. Peripheral neuropathy after occupational exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *American Journal of Industrial Medicine* 23:845-58.

82. Peper, M., M. Klett, R. Frentzel-Beyme, and W. D. Heller. 1993. Neuropsychological effects of chronic exposure to environmental dioxins and furans. *Environmental Research* 60:124-35.

83. Patterson Jr., D. G., M. A. Fingerhut, D. W. Roberts, L. L. Needham, M. H. Sweeney, D. A. Marlow, J. S. Andrews Jr., and W. E. Halperin. 1989. Levels of polychlorinated dibenzo-p-dioxins and dibenzofurans in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *American Journal of Industrial Medicine* 16:135-46.

84. Knapik, J. J., A. R. L. Burse, and J. A. Vogel. 1983. Height, weight, percent body fat, and indices of adiposity for young men and women entering the Army. *Aviation, Space, and Environmental Medicine* 54:223-31.

85. Jenkins, C. D., R. H. Roseman, and S. J. Zyzanski. 1974. Prediction of clinical coronary heart disease by a test for the coronary-prone behavior pattern. *New England Journal of Medicine* 290(23):1271-5.

86. Mausner, J. S., and A. K. Bahn. 1974. *Epidemiology – An Introductory Text.* Philadelphia: W. B. Saunders Company.

Table of Contents

List of Tables

10 NEOPLASIA ASSESSMENT

10.1 INTRODUCTION

10.1.1 Background

Between 1977 and 1988, numerous long-term exposure studies established the multi-organ carcinogenicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (dioxin) in experimental animals (1-8). The oncogenic response to dioxin occurs in multiple strains and species, in both sexes, and by several routes of administration: dermal (5), feeding (1, 2) and gavage (3, 4, 6), and intraperitoneal injection (7). Across a wide dose range and duration of exposure, dioxin can be considered a "complete" carcinogen solely responsible for a variety of malignant tumors at multiple sites (9). In rats, it has produced tumors of the liver, thyroid, adrenal cortex, lung, nasopharynx, tongue, brain, kidney, and breast (1, 2, 4); in mice, tumors of the liver, thymus, breast, stomach, and skin (3-6); and in the Syrian Hamster, a squamous cell carcinoma of the skin (7). The histopathologic characteristics of the neoplastic response demonstrated even greater variety—more than 30 distinct malignancies have been characterized microscopically (10).

As summarized in a recent review article (11), much of the basic research into the carcinogenicity of dioxin in laboratory animals has focused on the properties of the aryl hydrocarbon (Ah) receptor and the induction of the cytochrome P-450 enzyme system (11-17). The biologic basis for the assessment of risk related to dioxin exposure has been well established in molecular, biochemical, and pharmacologic studies and reviews (13, 18-24). The Ah receptor has been isolated from the tissues of several human organs (25-28) and the comparative properties of animal and human receptors have been studied (29, 30). These experiments have demonstrated far fewer Ah receptor sites and a significant reduction in dioxin binding affinity in human cells relative to rodent cell lines. These results suggest that at any level of exposure, humans may be less at risk for dioxin toxicity than laboratory animals (24).

Despite the conclusive evidence that dioxin is a potent carcinogen in animal experiments, the carcinogenicity of dioxin in humans remains controversial (31-36). The limitations of most epidemiological studies are well recognized and include the recall bias inherent in the retrospective collection of data, confounding by exposure to other potential toxins, histologic misclassification, and the lack of accurate indices of prior exposure to dioxin (31, 37, 38). Despite these limitations, the Institute of Medicine has concluded that there is "sufficient" evidence to establish an association, although not a causal relation, between dioxin exposure and the occurrence of soft tissue sarcoma (STS), non-Hodgkin's lymphoma, and Hodgkin's disease. The evidence for an association with respiratory cancers, prostate cancer, and multiple myeloma was considered "limited/suggestive" (39). Each of these malignancies is among the clinical endpoints included in mortality and morbidity data collected in this and previous examinations of the Air Force Health Study (AFHS).

Most of the longitudinal studies of dioxin toxicity have included malignancy as a clinical endpoint and have been based on cohorts of veterans who served during the Vietnam era (40-49) and of civilian populations exposed to dioxin by occupation (50-59) or as a consequence of industrial accidents (60-64). The development of assay techniques that quantitate the tissue concentration of dioxin in parts per quadrillion (65) and the validation of the reproducibility and reliability of the serum dioxin assay in parts per trillion (ppt) (66) have placed epidemiological studies of dioxin toxicity on a much more scientific footing. The serial analysis of serum dioxin levels from specimens taken 15 to 25 years after exposure has demonstrated that the best estimate for the half-life of dioxin in humans is 8.7 years (67). Although

an increasing number of published studies have incorporated serum dioxin levels into their analyses (68-73), few have examined the incidence of malignancy and associated mortality in relation to this index of dioxin exposure (44, 50, 52, 59, 60, 63).

As part of the National Institute of Occupational Safety and Health's (NIOSH) Dioxin Registry, cause-specific mortality was determined in 5,172 workers exposed to dioxin at chemical production plants (50). The mean dioxin level of 253 members of the exposed cohort was 233 ppt versus 7 ppt in the unexposed cohort. In the entire group of exposed workers, there was a slight but statistically significant increase in mortality from all cancers combined but not from those associated with dioxin exposure (non-Hodgkin's lymphoma, Hodgkin's disease, and STS). In a subcohort of 1,520 workers with longer exposure (greater than 1 year; mean serum dioxin of 418 ppt) and greater latency (more than 20 years since first exposure), there was a further increase in the mortality from all cancers combined (15% excess), a 42 percent excess of respiratory cancers, and a ninefold excess of STS sarcoma (35). In the most recently published report from the NIOSH study, which extended the period of observation for another 6 years through 1993, the standardized mortality ratio for all cancers combined in the cohort with the highest exposure was 1.60 and for lung cancer, 1.65 (74).

Although methodological limitations of the NIOSH study such as tissue classification (75), confounding (34, 61), and others (10) have been commented upon in the literature, some of the results are consistent with those of several other occupational epidemiological studies from Germany. In a 34-year follow-up of German factory workers exposed during a chemical explosion in 1953, the increase in mortality from all cancers combined was statistically significant only after a latency period of greater than 20 years (63). Similarly, in another mortality study of herbicide production workers who were followed over a 32-year period and whose exposure was verified by adipose tissue level (average dioxin level of 296 ng/kg), the increase in all-cancer mortality was significant only in those with more than 1-year exposure and latency period greater than 20 years. In this group, a significant increase in mortality was noted from both lung and hematopoietic cancers with a threefold increase in risk for non-Hodgkin's lymphoma (52). In the most recently published report of this study, the mortality follow-up was extended another 3 years and the significant increase in all-cancer mortality was confirmed (59). Taken together, the NIOSH and German studies are consistent with a carcinogenic effect of dioxin in humans with demonstrable dose-response and latency effects.

By far the most extreme human exposure to dioxin occurred consequent to the industrial explosion at Seveso, Italy, in 1976 (60, 64, 76, 77). In the population closest to the explosion (Zone A), serum levels of dioxin ranged from 828 ppt to 56,000 ppt, the highest ever recorded (78). In the most recent follow-up report published (60), residents of Zone B, farther from the source of contamination with serum dioxin levels ranging from 74 ppt to 526 ppt shortly after the accident, statistically significant increases in several cancers were noted, including primary hepatic and hematopoietic cancers and, particularly, non-Hodgkin's lymphoma in men and, in women, cancers of the gallbladder and biliary tree. The Seveso studies are limited by the small sample sizes (particularly in the group most heavily exposed), the limited data available on serum dioxin levels, and the lack of sufficient latency for the development of cancer.

In the incorporation of serial serum dioxin data into longitudinal analyses, the AFHS is unique among those that have examined the incidence of malignancy in Vietnam War veterans. During the 1992 examinations, after 10 years of observation, the median serum dioxin level in the Ranch Hand cohort was nearly three times that of the Comparison group (12.5 ppt versus 4.1 ppt) (44). Further, stratification of the Ranch Hand cohort by occupation revealed significantly higher median levels of serum dioxin in the enlisted groundcrew (24.1 ppt) and enlisted flyers (17.8 ppt) than in the officers (7.7 ppt).

In the 1992 follow-up examination, Ranch Hands continued to have a slightly higher history of benign and malignant skin neoplasms than Comparisons, but group differences were no longer significant. A

statistically significant inverse dose-response effect was noted, as basal cell skin cancer decreased as the level of serum dioxin increased. In contrast to the 1987 examinations, when Ranch Hands were found to have significantly more benign systemic neoplasms relative to Comparisons, in the 1992 examinations, the occurrence of benign systemic neoplasms was similar in each cohort with no evidence for a dose-response effect. There were no significant group differences in the morbidity or mortality associated with any systemic malignancy, nor was there any increased risk associated with current or initial levels of serum dioxin. In a recently published AFHS article, based on data collected through the 1992 examination, there was no significant increase in cancer risk in Ranch Hands with the highest levels of serum dioxin, nor was there any consistent evidence for a dose-response effect (79).

The term "neoplasm" is used throughout this report and refers to any new growth that may or may not be malignant. Malignant neoplasms are those neoplasms capable of invasion and metastasis. Malignant and benign neoplasms, carcinomas in situ, and neoplasms of uncertain behavior or unspecified nature, as well as skin and systemic neoplasms, were studied. "Systemic neoplasm" denotes a nonskin neoplasm.

10.1.2 Summary of Previous Analyses of the Air Force Health Study

10.1.2.1 1982 Baseline Study Summary Results

Cancer received major emphasis during the AFHS baseline examination in 1982. The neoplasia assessment used data from both the in-home questionnaire and the review-of-systems questionnaire obtained during the physical examination, as well as data from the examination itself. All data were verified by a medical records review. In addition, tabulation of mortality count data from the Baseline Mortality Report was used in conjunction with cancer morbidity information. The overall results did not show a significant difference in systemic cancer between the two groups, but did show significantly more skin cancer (p=0.03) in the Ranch Hand group.

Of 50 reported systemic cancers from the Ranch Hand and Comparison groups, 28 (14 in each group) were verified by medical records and pathology reports. A visual inspection of anatomic sites showed a slight excess of genitourinary cancer and oropharyngeal cancer but a relative deficit of digestive system neoplasms in Ranch Hands. A combined morbidity-mortality assessment derived from the initial 1:1 match (Ranch Hand to the Original Comparison member) disclosed similar distributions. One case of STS and one case of Hodgkin's disease were confirmed, both in the Comparison group.

Questionnaire data verified by a medical records review revealed significantly more skin cancer in Ranch Hands (odds ratio 2.35). Basal cell carcinoma accounted for 83.9 percent of the reported skin cancers in both groups and was concentrated anatomically on the face, head, and neck. The few melanoma and squamous cell cancers were distributed evenly between the Ranch Hand and Comparison groups. Skin cancer in both groups was associated with exposure to industrial chemicals (p=0.03). Adjustments for occupational exposures (e.g., asbestos, degreasing chemicals) did not alter the increased rate of skin cancer in the Ranch Hand group. Outdoor occupations subsequent to military service as a covariate did not account for the significant skin cancer association.

10.1.2.2 1985 Follow-up Study Summary Results

The baseline and 1985 follow-up data were combined for the assessment of lifetime history of cancer; occurrences of cancer prior to their service in Southeast Asia (SEA) were excluded.

For the unadjusted analyses (Blacks and non-Blacks included), Ranch Hands had a significantly greater frequency of a verified skin neoplasm (malignant, benign, or uncertain behavior or unspecified nature) than Comparisons. There were no significant unadjusted group differences in non-Black participants for

basal cell carcinoma, squamous cell carcinoma, melanoma, or all malignant skin neoplasms. For verified sun exposure-related malignant skin neoplasms, Ranch Hands had a marginally significantly greater frequency than Comparisons. The groups did not differ significantly for verified and suspected sun exposure-related malignant skin neoplasms. The adjusted group contrast for the sun exposure-related skin cancers, the majority of which were basal cell carcinomas, also was significant (p=0.030).

The unadjusted group contrasts for all systemic cancers combined were not significant. There was one new occurrence of an STS (Ranch Hand) and one suspected cancer of the lymphatic system (Ranch Hand), in addition to the one previously reported STS and one Hodgkin's disease in the Comparison group. There were no cases of non-Hodgkin's lymphoma in either group at the time of the 1985 report.

10.1.2.3 1987 Follow-up Study Summary Results

The unadjusted analysis of all verified neoplasms indicated that the proportion of Ranch Hands with a neoplasm was significantly greater than that of Comparisons. After including suspected neoplasms with verified neoplasms, the Ranch Hand proportion was marginally greater than the Comparison proportion. The majority of malignant neoplasms observed in Ranch Hands were basal cell carcinomas, a nonlife-threatening form of skin cancer. When the analysis was performed only on skin neoplasms for non-Black participants, significantly more Ranch Hands had a skin neoplasm than did Comparisons.

In the unadjusted analyses of verified basal cell carcinoma, a marginally significant group difference was found. After adjustment for age, residential history, sun exposure, ethnic background, and ionizing radiation exposure, the Ranch Hand risk was statistically significantly increased for verified basal cell carcinoma. Also, Ranch Hands had a significantly higher percentage of participants with multiple verified basal cell carcinomas than did Comparisons.

Sun exposure-related malignant skin neoplasms also exhibited group differences. (Approximately 90 percent of the participants with a sun exposure-related malignant neoplasm had a basal cell carcinoma.) In both the unadjusted and adjusted analyses, Ranch Hands exhibited a significantly increased risk for these neoplasms.

No significant group differences were found in the analyses of systemic neoplasms by number, behavior (malignant, benign, or uncertain behavior or unspecified nature), or site. Thus, the increase in overall malignancy was because of elevated relative risks for skin cancer (basal cell carcinoma). The number of STS and non-Hodgkin's lymphoma was comparable in the two groups.

10.1.2.4 Serum Dioxin Analysis of 1987 Follow-up Study Summary Results

The analyses generally did not establish a positive association between dioxin and the presence of a skin neoplasm. Significant relative risks were found for the skin neoplasm analyses; although, the relative risks were almost always less than 1.0. For the analyses focusing on enlisted flyers with a basal cell carcinoma of other sites (and a sun exposure-related malignant skin neoplasm of other sites), relative risks were found to be significant and greater than 1.0. These differences were not noted in the enlisted groundcrew who, as a group, had higher levels of serum dioxin than the enlisted flyers.

In general, the analyses of all systemic neoplasms combined produced some significant or marginally significant relative risks greater than 1.0. The relative risk for participants with a benign systemic neoplasm was significantly greater than 1.0. The relative risk of malignant systemic neoplasms was generally not significantly increased with increases in dioxin levels.

The study provided no evidence of increased history of malignant neoplasms most commonly suspected as being associated with exposure to chlorophenols (Hodgkin's disease, non-Hodgkin's lymphoma, and STS). The number of participants with these specific malignancies was small; therefore, the statistical power to detect small or moderately elevated relative risks was low. There is no evidence of a relation between dioxin and either skin or systemic malignancies in these data. There was a suggestion of a dose-response relation between dioxin and benign systemic neoplasms.

10.1.2.5 1992 Follow-up Study Summary Results

Analyses of all Ranch Hands and Comparisons indicated no significant difference between the two groups with regard to benign or malignant neoplasms. All statistically significant associations between initial dioxin and benign or malignant neoplasm endpoints for Ranch Hands showed an inverse dose-response relation. In the categorized dioxin analyses occurrence of neoplasms for Ranch Hands in the background and low dioxin categories was often greater than the occurrence for Comparisons before adjustment for covariates. After adjustment, the only significantly increased risks were for Ranch Hands in the low category (overall skin neoplasms and malignancies of the colon and rectum). In contrast, the occurrence of neoplasms of any type for Ranch Hands in the high dioxin category was never significantly elevated and was often less than the occurrence for Comparisons. Parallel to analyses using initial dioxin, results observed when current dioxin was used as the measure of exposure often indicated a negative dose-response relation, although this was statistically significant in the adjusted analyses only for benign skin neoplasms. In summary, there appeared to be no overall difference between Ranch Hands and Comparisons, and there was no evidence to suggest a positive dose-response relation between dioxin and neoplastic disease.

10.1.3 Parameters for the 1997 Neoplasia Assessment

10.1.3.1 Dependent Variables

The neoplasia assessment was based on the occurrence of neoplasms (both benign and malignant) after service in SEA. Information on the occurrence of neoplasms was indicated in the health questionnaires and the physical examinations at the 1982 baseline examination and at the 1985, 1987, and 1992 follow-up studies and was coded according to conventions in the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) manual. This information was combined with data collected at the 1997 follow-up examination to form a complete neoplastic history for each participant.

The neoplasia assessment was based on the number of participants with a neoplasm and not on the number of neoplasms. A participant was considered to have an adverse health condition for the neoplasia assessment if he had one or more neoplasms.

10.1.3.1.1 Medical Records Data

During the 1997 health interview, each study participant was asked a series of questions on the occurrence of cancer since the date of his last health interview. The self-reported conditions were verified by a medical records review and combined with cancer information collected at previous AFHS examinations. Only verified neoplasms were used in the neoplasia assessment.

Some possible neoplastic conditions were discovered by the physicians at the physical examination. Contingent upon participant authorization, suspicious skin lesions were biopsied and the pathology determined; no other invasive procedures were used to detect systemic neoplasms.

10.1.3.1.1.1 Skin Neoplasms

The analysis of skin neoplasms was divided into two sets. Analysis Set 1 consisted of analyses of skin neoplasms by behavior type. Four behavior types were examined: (1) all skin neoplasms, (2) malignant skin neoplasms only, (3) benign skin neoplasms only, and (4) skin neoplasms of uncertain behavior or unspecified nature.

Analysis Set 2 consisted of analyses of malignant skin neoplasms by cell type. The following four cell types were analyzed: (1) basal cell carcinomas, (2) squamous cell carcinomas, (3) nonmelanoma (basal cell carcinomas, squamous cell carcinomas, and malignant epithelial neoplasms not otherwise specified), and (4) melanoma. Analysis of basal cell carcinomas was conducted for all sites combined and by site. The following four sites were examined for basal cell carcinomas: (1) ear, face, head, and neck; (2) trunk; (3) upper extremities; and (4) lower extremities.

There were relatively few Black participants in this study (approximately 5%). With the exception of one Black participant with a pre-SEA melanoma, Blacks have been observed to exhibit only benign skin neoplasms in all phases of the study to date. Consequently, skin neoplasm analyses, except for the analyses of benign skin neoplasms, were limited to non-Blacks. Both Blacks and non-Blacks were included in the analysis of benign skin neoplasms. Participants with a pre-SEA skin neoplasm were excluded from the analysis of the skin neoplasm variables.

10.1.3.1.1.2 Systemic Neoplasms

The systemic neoplasms were analyzed by behavior and anatomical site. As with skin neoplasms, each analysis was conducted using verified data. The analysis of the systemic neoplasms was divided into two sets, described below.

Analysis Set 1 consisted of analyses of systemic neoplasms by behavior type. The following four behavior types were examined: (1) all systemic neoplasms, (2) malignant systemic neoplasms, (3) benign systemic neoplasms, and (4) systemic neoplasms of uncertain behavior or unspecified nature.

Analysis Set 2 consisted of analyses of malignant systemic neoplasms by the following sites: (1) ear, eye, head, face, and neck; (2) oral cavity, pharynx, and larynx; (3) esophagus; (4) brain; (5) thymus and mediastinum; (6) thyroid gland; (7) bronchus and lung; (8) liver; (9) colon and rectum; (10) kidney and bladder; (11) prostate; (12) testicles; (13) extrahepatic bile duct; (14) ill-defined sites; (15) connective and other soft tissues; and (16) carcinomas in situ of the penis.

In addition to the analyses described above, the number of participants with Hodgkin's disease, non-Hodgkin's lymphoma, and a malignant systemic neoplasm of lymphoid and histiocytic tissue was analyzed.

Participants with a pre-SEA malignant systemic neoplasm or a pre-SEA systemic neoplasm of uncertain behavior or an unspecified nature were excluded from the analysis of the systemic neoplasm variables.

10.1.3.1.1.3 Skin and Systemic Neoplasms

Statistical analysis was performed on all malignant neoplasms, which was a combination of malignant skin and malignant systemic neoplasms. In addition, statistical analysis was performed on all neoplasms, which was a combination of all skin and all systemic neoplasms (benign, malignant, and uncertain behavior). Participants with a pre-SEA skin neoplasm, a pre-SEA malignant systemic neoplasm, or a pre-SEA systemic neoplasm of uncertain behavior or an unspecified nature were excluded from the analysis of this variable.

10.1.3.1.2 Laboratory Examination Data

The prostate-specific antigen (PSA) test was developed to detect prostate enlargement and prostate cancer. Each participant had his PSA measured as a standard part of the laboratory assay. This measurement was continuous in nature, and the units were ng/ml. An analysis was performed on the continuous measurement, as well as on a discrete form. The discrete form of PSA was categorized as high or normal, based on a cutpoint of 4 ng/ml.

10.1.3.2 Covariates

In the analysis of the 1997 examination results, covariates in adjusted statistical analyses assessing skin neoplasms included age, military occupation, skin color, hair color, eye color, skin reaction to sun after the first exposure, skin reaction to sun after repeated exposure, lifetime exposure to ionizing radiation and industrial chemicals (yes or no), and average lifetime residential history. A composite skin-reaction index, which is a composite of the two individual reactions of skin to sun covariates, also was investigated.

Age, race, and military occupation were determined from military records. Information on skin, hair, and eye color was obtained at the 1997 physical examination for participants who did not attend the 1985, 1987, and 1992 examinations, and this information was combined with data from participants who previously provided this information. Information on the skin reaction to sun after the first exposure and after repeated exposure was reported by the participant during the questionnaire phase at the 1997 examination. Also, the participants' lifetime exposures through 1992 to ionizing radiation, industrial chemicals, and herbicides (used in the analysis of systemic neoplasms, discussed below) was updated with information reported in the 1997 questionnaire.

The emphasis on choosing risk factors related to cancer was increased during the 1985 follow-up study and has been emphasized since that time. In particular, the interval health questionnaire was modified to collect information on each geographic location in which a participant lived for more than 12 months. Because ultraviolet light exposure has been acknowledged as the primary cause of basal cell carcinomas, this information was used to compute a cumulative sun-exposure index based on residential history. An average lifetime residential history was estimated by dividing the total degree-years (i.e., the sum of the product of latitude [degrees] and the number of years lived at each residence) from all residences by the total number of residential years reported on questionnaires since 1985. Average lifetime residential history was dichotomized as less than 37 degrees latitude (southerly) or greater than or equal to 37 degrees latitude (northerly), which was the approximate median in previous AFHS examinations.

Covariates in adjusted statistical analyses assessing systemic neoplasms and PSA included age, race, lifetime exposure to ionizing radiation and herbicides, lifetime cigarette smoking history (in pack-years), and lifetime alcohol history (in drink-years).

Lifetime cigarette smoking history was based on questionnaire data. For lifetime cigarette smoking history, the respondent's average smoking was estimated over his lifetime based on his responses to the 1997 questionnaire, with 1 pack-year defined as 365 packs of cigarettes smoked during a single year.

Each participant was asked about his drinking patterns throughout his lifetime. When a participant's drinking patterns changed, he was asked to describe how his alcohol consumption differed and the duration of time that the drinking pattern lasted. The participant's average daily alcohol consumption was determined for each of the reported drinking pattern periods throughout his lifetime, and an estimate of the corresponding total number of drink-years was derived. One drink-year was the equivalent of drinking 1.5 ounces of an 80-proof alcoholic beverage, one 12-ounce beer, or one 5-ounce glass of wine per day for 1 year.

Almost all Ranch Hands reported herbicide exposure at some point in their lifetime (see Chapter 8, Covariate Associations with Estimates of Dioxin Exposure). Consequently, herbicide exposure in Ranch Hands was of limited use as a risk factor for explaining the presence of a systemic neoplasm. Therefore, many of the Model 2 and Model 4 analyses of systemic neoplasms and PSA, which were based on Ranch Hands only, did not use herbicide exposure as a covariate. Analyses that did not use herbicide exposure as a covariate are specified in footnotes to the table.

Categories of covariates and definitions are summarized below:

- Skin Color: dark, medium, pale, dark peach, and pale peach (classified for analysis purposes as (1) dark, medium, pale, or (2) dark peach, pale peach).
- Hair Color: black, dark brown, light brown, blonde, red, and bald (classified for analysis purposes as (1) black, dark brown, or (2) light brown, blonde, red, bald).
- Eye Color: brown, hazel, green, gray, and blue (classified for analysis purposes as (1) brown, (2) hazel, green, or (3) gray, blue).
- Skin Reaction to Sun After First Exposure: burns painfully, burns, becomes red, and no reaction.
- Skin Reaction to Sun After Repeated Exposure: freckles with no tan, tans mildly, tans moderately, and tans deep brown.
- Composite Skin-Reaction Index: a composite variable based on two reactions of skin to sun exposure variables was defined as follows: (1) burns painfully or freckles with no tan, (2) burns or tans mildly, and (3) all other reactions.
- Average Lifetime Residential History: average latitude less than 37 degrees and average greater than or equal to 37 degrees.
- Exposure to Carcinogens: ionizing radiation, industrial chemicals, and herbicides (yes or no for each). These exposures represent lifetime exposure based on self-reported questionnaire data from the 1997 examination combined with previous examinations.

10.1.4 Statistical Methods

Table 10-1 summarizes the statistical analysis performed for the neoplasia assessment. The first part of this table identifies the dependent variables, covariates, exclusions, and the statistical methods. This information is presented in the following four sections: skin neoplasms, systemic neoplasms, skin and systemic neoplasms combined, and PSA. Data source, data form, and cutpoints are summarized at the end of the table. The second part of the table describes the covariates. A covariate was used in its continuous form whenever possible for all adjusted analyses; if necessary, or if the covariate was inherently discrete (e.g., military occupation), or if a categorized form was needed to develop measures of association with the dependent variable, the covariate was categorized as shown in Table 10-1.

Table 10-1. Statistical Analysis for the Neoplasia Assessment

Dependent Variables

Category	Site	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
Skin Neoplasms				
Behavior				
All	All Sites Combined	(1)	(a)	U:LR A:LR
Malignant	All Sites Combined	(1)	(a)	U:LR A:LR L:LR
Benign	All Sites Combined	(1)	(b)	U:LR A:LR
Uncertain Behavior or Unspecified Nature	All Sites Combined	(1)	(a)	U:LR,CS A:LR
Cell Type and Site				
Basal Cell Carcinoma	All Sites Combined Ear, Face, Head, and Neck Trunk Upper Extremities Lower Extremities	(1)	(a)	U:LR A:LR
Squamous Cell Carcinoma	All Sites Combined	(1)	(a)	U:LR A:LR
Nonmelanoma	All Sites Combined	(1)	(a)	U:LR A:LR
Melanoma	All Sites Combined	(1)	(a)	U:LR,CS A:LR
Systemic Neoplasms				
Behavior				
All	All Sites Combined	(2)	(c)	U:LR A:LR
Malignant	All Sites Combined	(2)	(c)	U:LR A:LR L:LR
Benign	All Sites Combined	(2)	(c)	U:LR A:LR L:LR
Uncertain Behavior or Unspecified Nature	All Sites Combined	(2)	(c)	U:LR A:LR
Site				
Malignant	Eye, Ear, Face, Head, and Neck	(2)	(c)	U:LR A:LR
Malignant	Oral Cavity, Pharynx, and Larynx	(2)	(c)	U:LR A:LR

Table 10-1. Statistical Analysis for the Neoplasia Assessment (Continued)

Category	Site	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
Malignant	Esophagus	--	(c)	Descriptive
Malignant	Brain	--	(c)	Descriptive
Malignant	Thymus, Heart, and Mediastinum	(2)	(c)	U:LR,CS A:LR
Malignant	Thyroid Gland	(2)	(c)	U:LR,CS A:LR
Malignant	Bronchus and Lung	(2)	(c)	U:LR,CS A:LR
Malignant	Liver	(2)	(c)	U:LR,CS A:LR
Malignant	Colon and Rectum	(2)	(c)	U:LR A:LR
Malignant	Kidney and Bladder	(2)	(c)	U:LR,CS A:LR
Malignant	Prostate	(2)	(c)	U:LR A:LR
Malignant	Testicles	(2)	(c)	U:LR,CS A:LR
Malignant	Extrahepatic Bile Duct	--	(c)	Descriptive
Malignant	Ill-Defined Sites	--	(c)	Descriptive
Malignant	Connective and Other Soft Tissues	(2)	(c)	U:LR,CS A:LR
Carcinoma In Situ	Penis	--	(c)	Descriptive
Hodgkin's Disease	--	(2)	(c)	U:LR,CS A:LR
Non-Hodgkin's Lymphoma	--	(2)	(c)	U:LR,CS A:LR
Other Malignant Systemic Neoplasms of Lymphoid and Histiocytic Tissue	--	(2)	(c)	U:LR,CS A:LR
Skin and Systemic Neoplasms				
All	All Sites Combined	(3)	(d)	U:LR A:LR

Variable (Units)	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
Prostate-Specific Antigen					
Prostate-Specific Antigen (ng/ml)	D/C	High: >4 Normal: ≤4	(2)	(e)	U:LR,GLM A:LR,GLM

Dependent Variables (Except for PSA)

Data Source: Review of medical records and verification based on AFHS 1997 follow-up questionnaires and physical examinations, except for PSA, which was measured by Scripps Clinic in 1997.
Data Form: Discrete.
Cutpoints: Yes or No.

Table 10-1. Statistical Analysis for the Neoplasia Assessment (Continued)

[a] Covariates:
(1): age, military occupation, skin color, hair color, eye color, skin reaction to sun after first exposure, skin reaction to sun after repeated exposure, composite skin-reaction index, residential history, ionizing radiation exposure, and industrial chemicals exposure.
(2): age, race, military occupation, ionizing radiation exposure, herbicide exposure, lifetime cigarette smoking history, lifetime alcohol history.
(3): age, race, military occupation, skin color, hair color, eye color, skin reaction to sun after first exposure, skin reaction to sun after repeated exposure, composite skin-reaction index, residential history, ionizing radiation exposure, industrial chemicals exposure, herbicide exposure, lifetime cigarette smoking history, lifetime alcohol history.

[b] Exclusions:
(a): participants with pre-SEA skin neoplasms, Blacks.
(b): participants with pre-SEA skin neoplasms.
(c): participants with pre-SEA uncertain behavior neoplasms, participants with pre-SEA malignant systemic neoplasms.
(d): participants with pre-SEA skin neoplasms, participants with pre-SEA uncertain behavior neoplasms, participants with pre-SEA malignant systemic neoplasms.
(e): participants with a prostatectomy or radiation treatment on the prostate gland.

Covariates

Variable (Units)	Data Source	Data Form	Cutpoints
Age (years)	MIL	D/C	Born ≥1942 Born <1942
Race	MIL	D	Black Non-Black
Occupation	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Skin Color	PE	D	Non-Peach: Dark, Medium, Pale Peach: Dark Peach, Pale Peach
Hair Color	PE	D	Black, Dark Brown Light Brown, Blonde, Red, Bald
Eye Color	PE	D	Brown Hazel, Green Gray, Blue
Skin Reaction to Sun After First Exposure	Q-SR	D	Burns Painfully Burns Becomes Red No Reaction
Skin Reaction to Sun After Repeated Exposure	Q-SR	D	Freckles with No Tan Tans Mildly Tans Moderately Tans Deep Brown

Table 10-1. Statistical Analysis for the Neoplasia Assessment (Continued)

Variable (Units)	Data Source	Data Form	Cutpoints
Composite Skin-Reaction Index	Q-SR	D	• Burns Painfully After 2 Hours, or Freckles with No Tan After Repeated Exposure • Burns After 2 Hours, or Tans Mildly After Repeated Exposure • All Other Reactions
Average Lifetime Residential History	Q-SR	D	Latitude <37° Latitude ≥37°
Ionizing Radiation Exposure	Q-SR	D	Yes No
Industrial Chemicals Exposure	Q-SR	D	Yes No
Herbicide Exposure	Q-SR	D	Yes No
Lifetime Cigarette Smoking History (pack-years)	Q-SR	D/C	0 >0-10 >10
Lifetime Alcohol History (drink-years)	Q-SR	D/C	0 >0-40 >40

Abbreviations

Data Source: MIL: Air Force military records
PE: 1997 physical examination
Q-SR: Health questionnaires (self-reported)

Data Form: D: Discrete analysis only
D/C: Discrete and continuous analysis for dependent variables; appropriate form for analysis (either discrete or continuous) for covariates

Statistical Analysis: U: Unadjusted analysis
A: Adjusted analysis
L: Longitudinal analysis

Statistical Methods: CS: Chi-square contingency table analysis (continuity-adjusted for 2x2 tables)
GLM: General linear models analysis
LR: Logistic regression analysis

Many covariates were available for use in adjusted analyses of skin and systemic neoplasms. In addition, the number of neoplasms was small for many of the dependent variables. The modeling strategy for this clinical area was to include as many covariates as feasible. When the number of participants with a history of a particular neoplasm was too small to support analysis including all covariates, elimination of covariates was necessary to develop and support meaningful analysis. The covariates that were removed from analysis for a given health endpoint and model are specified in footnotes to the table.

Table 10-2 provides a summary of the number of participants with missing covariate data. In addition, the number of participants excluded is provided.

Table 10-2. Number of Participants Excluded or with Missing Data for the Neoplasia Assessment

		Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
Variable	Variable Use	Ranch Hand	Comparison	Initial	1987	Ranch Hand	Comparison
Hair Color	COV	0	2	0	0	0	2
Skin Reaction to Sun after First Exposure	COV	1	0	0	1	1	0
Skin Reaction to Sun after Repeated Exposure	COV	1	0	0	1	1	0
Composite Skin-Reaction Index	COV	1	0	0	1	1	0
Lifetime Cigarette Smoking History	COV	2	1	1	2	2	1
Lifetime Alcohol History	COV	6	2	3	6	6	1
Blacks	EXC	55	73	36	55	55	70
Pre-SEA Skin Neoplasm	EXC	10	11	7	10	10	11
Pre-SEA Malignant Systemic Neoplasm	EXC	5	0	4	5	5	0
Pre-SEA Systemic Neoplasm of Uncertain Behavior	EXC	5	2	3	5	5	2
Prostatectomy or Radiation Treatment on Prostate Gland	EXC	41	61	24	40	40	61

Note: COV = Covariate.
EXC = Exclusion.
870 Ranch Hands and 1,251 Comparisons.
482 Ranch Hands for initial dioxin; 863 Ranch Hands for 1987 dioxin.
863 Ranch Hands and 1,213 Comparisons for categorized dioxin.

10.1.4.1 Longitudinal Analysis

Longitudinal analysis of malignant skin neoplasms, malignant systemic neoplasms, and benign systemic neoplasms was conducted to evaluate the association between exposure and the change in neoplasm status between the 1982 baseline examination and the 1997 follow-up examination.

10.2 RESULTS

10.2.1 Dependent Variable-Covariate Associations

The associations between the dependent variables examined in the neoplasia assessment and the covariates used in the adjusted analyses were investigated, and the results are presented in Appendix F, Table F-2. These associations are pairwise between the dependent variable and the covariate and are not adjusted for any other covariates. The exclusions specified in Table 10-1 were used in the dependent variable-covariate associations described below.

Tests of covariate association were conducted for any skin neoplasm and malignant skin neoplasms. Results were similar for both variables. Significant associations with age ($p<0.001$ for both) were found, where older participants displayed a greater history of a skin neoplasm or a malignant skin neoplasm than did younger participants. Significant associations also were found with occupation ($p=0.004$ and $p<0.001$, respectively). More benign or malignant skin neoplasms were found for officers, followed by enlisted flyers, and then enlisted groundcrew. Skin color was associated with skin neoplasms and malignant skin neoplasms ($p<0.001$ and $p=0.003$, respectively). A higher percentage of skin neoplasms was found for participants with peach-colored skin as compared to participants with non-peach-colored skin. A significant association also was found between malignant skin neoplasms and hair color ($p=0.025$). More participants with light brown, blonde, or red hair had malignant skin neoplasms than did participants with black or dark brown hair. Eye color displayed a significant association with both variables ($p=0.026$ and $p=0.023$ for any skin neoplasm and any malignant skin neoplasm, respectively). Participants with brown eyes exhibited the smallest percentage of skin neoplasms.

Significant associations also were found between any skin and malignant skin neoplasms and both sun reaction covariates ($p<0.001$ for each). The percentage of participants with skin neoplasms increased as the levels of sun sensitivity increased for both covariates. In addition, the composite skin-reaction index displayed significant associations with both variables ($p<0.001$ for both). For the skin-reaction index, the skin neoplasms and malignant skin neoplasms increased as the reaction to sun increased. The associations with average lifetime residential history were significant ($p=0.017$ and $p<0.001$, respectively). The occurrence of both types of neoplasms was greater for those participants who had lived in more southerly latitudes than in the northern latitudes. Ionizing radiation exposure also displayed significant associations with both variables ($p=0.002$ and $p=0.031$, respectively). More skin neoplasms and malignant skin neoplasms were observed for those participants who reported exposure to ionizing radiation than for those who did not report exposure.

Results from the covariate association tests for benign skin neoplasms were significant only for skin color ($p=0.025$). Participants with peach-colored skin showed more benign skin neoplasms (24.6%) than did participants with non-peach-colored skin (19.8%).

The covariate association test results for (a) any basal cell carcinoma and (b) basal cell carcinoma of the ear, face, head, or neck were similar. Each variable displayed a significant association with age and occupation ($p<0.001$ for each association). The history of a basal cell carcinoma was higher for older participants and highest for officers. Associations with skin color were also significant for both basal cell carcinoma variables ($p=0.019$ and $p=0.018$, respectively), revealing more basal cell carcinomas for participants with peach-colored skin than for participants with non-peach-colored skin. Hair color also was associated significantly with both variables ($p=0.019$ and $p=0.005$). Participants with lighter hair colors displayed more of the two basal cell carcinoma dependent variables than did participants with darker hair colors. Basal cell carcinoma was significantly associated with eye color ($p=0.034$). The smallest percentage of participants with basal cell carcinoma was for those with brown eyes.

Significant associations with any basal cell carcinoma and basal cell carcinoma of the ear, face, head, or neck also were found for both sun reaction covariates ($p<0.001$ for each). Basal cell carcinomas increased as the levels of sun sensitivity increased. In addition, the composite skin-reaction index displayed significant associations with both covariates ($p<0.001$ for both), where basal cell carcinoma increased as the reaction to sun increased. Significant associations also were found for both variables with the average lifetime residential history ($p<0.001$ for both variables). The occurrence of basal cell carcinoma was greater for participants who had lived in the more southerly latitudes. A significant association with ionizing radiation exposure was found for basal cell carcinoma of the ear, face, head, or

neck ($p=0.049$). This association revealed more basal cell carcinomas for participants reporting exposure to ionizing radiation.

Tests of covariate association conducted for basal cell carcinoma on the trunk and basal cell carcinoma on the upper extremities showed similar results. Each variable was associated significantly with age ($p=0.007$ and $p=0.031$, respectively). Older participants had more basal cell carcinomas on the trunk and upper extremities than did younger participants. Occupation was also a significant covariate ($p<0.001$ for both). Officers had more basal cell carcinomas of the trunk or upper extremities. Eye color was associated significantly with basal cell carcinoma of the upper extremities ($p=0.005$). Participants with hazel or green eyes had more basal cell carcinomas.

Significant associations with basal cell carcinoma of the trunk and basal cell carcinoma of the upper extremities were also found for both skin reaction to sun after the first exposure ($p=0.006$ and $p<0.001$, respectively) and skin reaction to sun after repeated exposure ($p<0.001$ for both dependent variables). The occurrence of basal cell carcinomas increased as the sensitivity to sun increased. In addition, the composite skin-reaction index displayed significant associations with both variables ($p<0.001$ for both basal cell carcinoma variables), where basal cell carcinoma of the trunk or upper extremities increased as the sensitivity to sun increased. Significant associations also were found for both basal cell carcinoma variables with average lifetime residential history ($p<0.001$ and $p=0.039$, respectively). Basal cell carcinoma of the trunk or upper extremities was higher for participants who had lived in the more southerly latitudes.

Tests of association for squamous cell carcinoma showed several significant findings. A significant association with age ($p=0.002$) displayed more squamous cell carcinomas for older participants (3.0%) than for younger participants (0.9%). The association with occupation also was significant ($p=0.007$). More squamous cell carcinomas were found for officers (3.3%), then enlisted flyers (1.6%), and enlisted groundcrew (1.2%). The associations with both skin reaction to sun covariates also were significant ($p=0.011$ for reaction after first exposure and $p<0.001$ for reaction after repeated exposure). Both skin reaction to sun covariates displayed more squamous cell carcinomas as skin sensitivity to sun increased. The composite skin-reaction index association with squamous cell carcinoma was significant ($p<0.001$). Squamous cell carcinoma increased as the reaction to sun increased. Squamous cell carcinoma for participants who had lived in the more southerly latitudes had occurred more often than for participants who had lived in the northern latitudes ($p=0.009$).

Several covariates were associated significantly with nonmelanoma. Significantly more nonmelanomas ($p<0.001$) were observed in older participants (20.3%) than in younger participants (9.7%). Nonmelanoma also was associated significantly with occupation ($p<0.001$). Nonmelanoma was highest for officers (20.0%), then enlisted flyers (16.0%), and enlisted groundcrew (11.5%). The significant association between nonmelanoma and skin color ($p=0.003$) displayed more nonmelanoma for participants with peach-colored skin than for participants with non-peach-colored skin (17.1% vs. 11.2%). The association between nonmelanoma and hair color was significant ($p=0.016$). Those participants with lighter hair colors exhibited more nonmelanomas (18.7%) compared to those with darker hair colors (14.4%). A significant association between nonmelanoma and eye color showed a smaller percentage of nonmelanoma in participants with brown eyes ($p=0.039$).

Both skin reaction to sun covariates were significant ($p<0.001$ for both covariates) and showed more nonmelanomas as the skin sensitivity to sun increased. The composite skin-reaction index association with nonmelanoma also was significant ($p<0.001$). Nonmelanoma increased as the reaction to sun increased. Nonmelanomas were significantly greater for participants who had lived in more southerly latitudes ($p<0.001$).

A significant association between melanoma and average lifetime residential history was observed (p=0.008). Melanoma was significantly greater for participants who had lived in more northerly latitudes.

Tests of covariate association for any systemic neoplasm were significant for age (p<0.001), occupation (p=0.008), and herbicide exposure (p=0.003). A history of systemic neoplasms was higher for older participants (37.2%) than for younger participants (21.8%). Officers displayed the largest occurrence of a systemic neoplasm (33.9%), followed by enlisted flyers (31.1%), then enlisted groundcrew (27.1%). In addition, participants reporting exposure to herbicides exhibited more systemic neoplasms (32.7%) compared to those who did not report exposure to herbicides (26.4%).

Several covariates displayed a significant association with malignant systemic neoplasms. Age was significant (p<0.001), with older participants showing more malignant systemic neoplasms (10.2%) than younger participants (2.4%). A significant association between malignant systemic neoplasms and occupation was found (p<0.001), with the largest occurrence in officers (8.6%) and enlisted flyers (8.6%), followed by enlisted groundcrew (4.4%). The association with ionizing radiation exposure also was significant (p=0.004). For participants who had reported exposure to ionizing radiation, 9.5 percent had a malignant systemic neoplasm compared to 5.8 percent of participants who had not reported exposure. The association between malignant systemic neoplasms and herbicide exposure was significant (p=0.004). Participants who had reported being exposed to herbicides had more malignant systemic neoplasms (8.0%) than participants who had not reported being exposed (4.6%). Lifetime cigarette smoking history also was associated significantly with malignant systemic neoplasms (p<0.001). Participants who had smoked the heaviest (in terms of pack-years) had more malignant systemic neoplasms.

Benign systemic neoplasms displayed significant associations with age (p<0.001) and herbicide exposure (p=0.045). Older participants exhibited more benign systemic neoplasms (28.9%) than did younger participants (19.2%). A greater percentage of participants who had reported being exposed to herbicides had more benign systemic neoplasms (26.1%) than those participants who had not reported exposure to herbicides (22.1%).

Covariate association tests with systemic neoplasms of uncertain behavior or unspecified nature revealed a significant result for occupation (p=0.031). Officers displayed the most systemic neoplasms of uncertain behavior or unspecified nature (2.9%), followed by enlisted groundcrew (1.5%), then enlisted flyers (0.9%).

A significant association between age and a malignant systemic neoplasm of the eye, ear, face, head, or neck was found (p=0.035). Older participants had more malignant systemic neoplasms of the eye, ear, face, head, or neck (1.4%) than did younger participants (0.4%).

Tests of covariate association for malignant systemic neoplasms of the oral cavity, pharynx, and larynx were significant for age (p=0.041). Older participants displayed more malignant systemic neoplasms of the oral cavity, pharynx, and larynx (0.9%) than did younger participants (0.1%).

Malignant systemic neoplasms of the bronchus and lung were associated significantly with lifetime cigarette smoking history (p<0.001). Only participants who had smoked the most (>10 pack-years) showed a malignant systemic neoplasm of the bronchus or lung (1.4%).

Several significant results were revealed from the covariate association tests conducted for malignant systemic neoplasms of the kidney and bladder. A significant association with age (p=0.014) showed more malignant systemic neoplasms of the kidney or bladder in older participants (1.3%) than in younger

participants (0.2%). The association with lifetime cigarette smoking history was significant ($p<0.001$). Malignant systemic neoplasms of the kidney or bladder increased with smoking. The association with lifetime alcohol history also was significant ($p<0.001$). The greatest percentage of participants with malignant systemic neoplasms of the kidney or bladder was for non-drinkers (3.4%).

Tests of covariate association for malignant systemic neoplasms of the prostate revealed several significant results. Older participants had significantly more ($p<0.001$) malignant systemic neoplasms of the prostate (5.3%) than did younger participants (0.2%). A significant association with occupation ($p=0.002$) revealed more malignant systemic neoplasms of the prostate in officers (4.6%), followed by enlisted flyers (3.3%), then enlisted groundcrew (1.7%). A significant result also was found with ionizing radiation exposure ($p=0.044$). For participants reporting exposure to ionizing radiation, 4.5 percent had a malignant systemic neoplasm of the prostate, compared to 2.6 percent who did not report exposure. Results also were significant for the tests of association with herbicide exposure ($p=0.035$). The percentage of participants reporting exposure to herbicides with malignant systemic neoplasms was 3.7 percent, compared to 2.0 percent who did not report exposure to herbicides. Lifetime cigarette smoking history showed a significant association with malignant systemic neoplasms of the prostate ($p=0.017$). The greatest occurrence of malignant systemic neoplasms of the prostate was for participants who had smoked the most (4.1%).

Covariate association tests conducted for all malignant skin and systemic neoplasms and all skin and systemic neoplasms were similar. Age, race, and occupation each were significant for both variables ($p<0.001$ for each test). Older participants showed more neoplasms for both variables than did younger participants. Skin and systemic neoplasms occurred more often in non-Blacks than in Blacks. Officers showed more skin and systemic neoplasms than did enlisted flyers and enlisted groundcrew. Skin color was associated significantly with both dependent variables ($p<0.001$ for each). Participants with peach-colored skin had more skin and systemic neoplasms than did participants with non-peach-colored skin. The association between hair color and all malignant skin and systemic neoplasms was significant ($p<0.001$). Participants who had lighter hair colors had more malignant skin or systemic neoplasms. Eye color associations for both variables were each significant ($p<0.001$ for both tests). Participants with brown eyes showed the smallest occurrence of a skin or systemic neoplasm.

Significant associations with all malignant skin and systemic neoplasms and all skin and systemic neoplasms also were found for both skin reaction to sun and the composite skin-reaction index covariates ($p<0.02$ for all tests). Skin or systemic neoplasms increased as skin sensitivity to the sun increased. A significant association also was found for all malignant skin and systemic neoplasms with the average lifetime residential history covariate ($p<0.001$). Malignant skin or systemic neoplasms occurred more often for participants who lived in more southerly latitudes. The ionizing radiation exposure and herbicide exposure covariate tests were each significant for both variables ($p<0.02$ for all tests). Participants reporting exposure to either ionizing radiation or herbicides displayed more skin and systemic neoplasms (both malignant systemic neoplasms and all systemic neoplasms combined) than did participants who did not report exposure.

Covariate association tests for both the continuous and discrete forms of PSA were significant for age ($p<0.001$ for PSA in both discrete and continuous forms) and occupation ($p<0.001$, continuous, and $p=0.014$, discrete). PSA levels and the proportion of participants with high PSA levels increased with age. Enlisted groundcrew showed the lowest average levels of PSA and the lowest percentage of participants with high PSA levels.

10.2.2 Exposure Analysis

The following section presents results of the statistical analysis of the dependent variables shown in Table 10-1. Dependent variables were derived from a medical records review and verification and a laboratory measurement of PSA at the 1997 follow-up examination.

Four models were examined for each dependent variable given in Table 10-1. The analyses of these models are presented below. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7, respectively. These analyses were performed both unadjusted and adjusted for relevant covariates. Model 1 examined the relation between the dependent variable and group (i.e., Ranch Hand or Comparison). In this model, exposure was defined as "yes" for Ranch Hands and "no" for Comparisons without regard to the magnitude of the exposure. As an attempt to quantify exposure, three contrasts of Ranch Hands and Comparisons were performed along with the overall Ranch Hand versus Comparison contrast. These three contrasts compared Ranch Hands and Comparisons within each occupational category (officers, enlisted flyers, and enlisted groundcrew). As described in Table 2-8 and previous reports, the average levels of exposure to dioxin were highest for enlisted groundcrew, followed by enlisted flyers, then officers.

Model 2 explored the relation between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt. If a participant did not have a 1987 dioxin level, the 1992 level was used to estimate the initial dioxin level. If a participant did not have a 1987 or a 1992 dioxin level, the 1997 level was used to estimate the initial dioxin level. A statistical adjustment for the percentage of body fat at the time of the participant's blood measurement of dioxin was included in this model to account for body-fat-related differences in elimination rate (80).

Model 3 divided the Ranch Hands examined in Model 2 into two categories based on their initial dioxin measures. These two categories are referred to as "low Ranch Hand" and "high Ranch Hand." Two additional categories, Ranch Hands with 1987 serum dioxin levels at or below 10 ppt and Comparisons with 1987 serum dioxin levels at or below 10 ppt, were formed and included in the model. Ranch Hands with 1987 serum dioxin levels at or below 10 ppt are referred to as the "background Ranch Hand" category. Dioxin levels in 1992 were used if the 1987 level was not available, and dioxin levels in 1997 were used if the 1987 and 1992 levels were not available. These four categories—Comparisons, background Ranch Hands, low Ranch Hands, and high Ranch Hands—were used in Model 3 analyses. The relation between the dependent variable in each of the three Ranch Hand categories and the dependent variable in the Comparison category was examined. A fourth contrast, exploring the relation of the dependent variable in the combined low and high Ranch Hand categories relative to Comparisons, also was conducted. This combination is referred to in the tables as the "low plus high Ranch Hand" category. As in Model 2, a statistical adjustment for the percentage of body fat at the time of the participant's blood measurement of dioxin was included in this model.

Model 4 examined the relation between the dependent variable and 1987 lipid-adjusted dioxin levels in all Ranch Hands with a dioxin measurement. If a participant did not have a 1987 dioxin measurement, the 1992 measurement was used to determine the dioxin level. If a participant did not have a 1987 or a 1992 dioxin measurement, the 1997 measurement was used to determine the dioxin level.

Some participants had multiple neoplasms, and a participant may be represented in more than one table; therefore, totals added across tables may not agree. For example, 496 of the 2,121 participants in this study (29.8%) had at least two neoplasms and 94 (10.8%) had at least two malignant neoplasms.

10.2.2.1 Medical Records Review

10.2.2.1.1 Skin Neoplasms (All Sites Combined)

Significant group differences were found for all occupations combined and within the officer and enlisted flyer occupational strata in both the Model 1 unadjusted and adjusted analyses of a history of skin neoplasms (Table 10-3(a,b): Est. RR=1.29, p=0.007; Adj. RR=1.32, p=0.005, for all occupations; Est. RR=1.36, p=0.034; Adj. RR=1.38, p=0.030, for officers; and Est. RR=1.64, p=0.040; Adj. RR=1.66, p=0.040, for enlisted flyers). Each contrast displayed more Ranch Hands than Comparisons with skin neoplasms. Results were nonsignificant for the enlisted groundcrew contrasts (p>0.33 for both the unadjusted and adjusted analyses).

Table 10-3. Analysis of Skin Neoplasms

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***805***	***325 (40.4)***	***1.29 (1.07,1.55)***	***0.007***
	Comparison	***1,168***	***402 (34.4)***		
Officer	Ranch Hand	329	150 (45.6)	1.36 (1.02,1.81)	0.034
	Comparison	480	183 (38.1)		
Enlisted Flyer	Ranch Hand	140	56 (40.0)	1.64 (1.02,2.63)	0.040
	Comparison	173	50 (28.9)		
Enlisted Groundcrew	Ranch Hand	336	119 (35.4)	1.12 (0.84,1.50)	0.433
	Comparison	515	169 (32.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.32 (1.09,1.60)***	***0.005***
Officer	1.38 (1.03,1.85)	0.030
Enlisted Flyer	1.66 (1.02,2.69)	0.040
Enlisted Groundcrew	1.16 (0.86,1.56)	0.339

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	138	63 (45.7)	0.78 (0.67,0.91)	0.001
Medium	150	64 (42.7)		
High	151	42 (27.8)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

Table 10-3. Analysis of Skin Neoplasms (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
439	0.81 (0.68,0.98)	0.028

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,133	389 (34.3)		
Background RH	359	155 (43.2)	1.49 (1.17,1.90)	0.001
Low RH	210	94 (44.8)	1.54 (1.14,2.07)	0.005
High RH	229	75 (32.8)	0.91 (0.67,1.23)	0.546
Low plus High RH	439	169 (38.5)	1.17 (0.93,1.47)	0.183

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,131		
Background RH	358	1.46 (1.13,1.88)	0.004
Low RH	210	1.49 (1.10,2.04)	0.011
High RH	229	1.05 (0.76,1.45)	0.747
Low plus High RH	439	1.25 (0.98,1.58)	0.073

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 10-3. Analysis of Skin Neoplasms (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	273	114 (41.8)	0.88 (0.80,0.97)	0.012
Medium	256	120 (46.9)		
High	269	90 (33.5)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
797	0.92 (0.82,1.03)	0.147

[a] Relative risk for a twofold increase in 1987 dioxin.

Results from both the unadjusted and adjusted Model 2 analyses indicated a significant inverse relation between initial dioxin and skin neoplasms (Table 10-3(c,d): Est. RR=0.78, p=0.001; Adj. RR=0.81, p=0.028, respectively). As initial dioxin in Ranch Hands increased, the occurrence of skin neoplasms decreased.

The Model 3 analyses contrasting Ranch Hands in both the background dioxin category and low dioxin category with Comparisons displayed significant results in the unadjusted and adjusted analyses of skin neoplasms (Table 10-3(e,f): Est. RR=1.49, p=0.001; Adj. RR=1.46, p=0.004; and Est. RR=1.54, p=0.005; Adj. RR=1.49, p=0.011, respectively). A marginally significant difference between Ranch Hands in the low plus high dioxin category and Comparisons was revealed in the adjusted analysis of skin neoplasms (Table 10-3(f): Adj. RR=1.25, p=0.073). Each contrast displayed more Ranch Hands than Comparisons with skin neoplasms. All other Model 3 contrasts were nonsignificant (Table 10-3(e,f): p>0.18).

The Model 4 unadjusted analysis revealed a significant inverse relation between skin neoplasms and 1987 dioxin levels (Table 10-3(g): Est. RR=0.88, p=0.012). After adjustment for covariates, the association was nonsignificant (Table 10-3(h): p=0.147).

10.2.2.1.2 Malignant Skin Neoplasms

The Model 1 enlisted flyer contrast revealed a marginally significantly higher percentage of a history of malignant skin neoplasms for Ranch Hands than for Comparisons in both the unadjusted and adjusted analyses (Table 10-4(a,b): Est. RR=1.79, p=0.059; Adj. RR=1.86, p=0.055, respectively). All other Model 1 contrasts were nonsignificant (Table 10-4(a,b): p>0.16).

Table 10-4. Analysis of Malignant Skin Neoplasms

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***805***	***144 (17.9)***	***1.14 (0.90,1.45)***	***0.274***
	Comparison	***1,168***	***187 (16.0)***		
Officer	Ranch Hand	329	77 (23.4)	1.24 (0.88,1.74)	0.218
	Comparison	480	95 (19.8)		
Enlisted Flyer	Ranch Hand	140	29 (20.7)	1.79 (0.98,3.29)	0.059
	Comparison	173	22 (12.7)		
Enlisted Groundcrew	Ranch Hand	336	38 (11.3)	0.81 (0.53,1.24)	0.329
	Comparison	515	70 (13.6)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.19 (0.93,1.54)***	***0.175***
Officer	1.29 (0.90,1.85)	0.161
Enlisted Flyer	1.86 (0.99,3.51)	0.055
Enlisted Groundcrew	0.86 (0.56,1.34)	0.509

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	138	31 (22.5)	0.79 (0.64,0.96)	0.015
Medium	150	30 (20.0)		
High	151	18 (11.9)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
n	Analysis Results for Log_2 (Initial Dioxin) Adjusted Relative Risk (95% C.I.)[a]	p-Value
439	0.87 (0.68,1.12)	0.287

[a] Relative risk for a twofold increase in initial dioxin.

Table 10-4. Analysis of Malignant Skin Neoplasms (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,133	179 (15.8)		
Background RH	359	65 (18.1)	1.21 (0.88,1.66)	0.237
Low RH	210	47 (22.4)	1.52 (1.06,2.19)	0.023
High RH	229	32 (14.0)	0.84 (0.56,1.27)	0.417
Low plus High RH	439	79 (18.0)	1.12 (0.83,1.51)	0.457

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,131		
Background RH	358	1.13 (0.81,1.58)	0.476
Low RH	210	1.45 (0.98,2.14)	0.062
High RH	229	1.19 (0.76,1.85)	0.453
Low plus High RH	439	1.30 (0.95,1.80)	0.104

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	273	48 (17.6)	0.92 (0.81,1.04)	0.187
Medium	256	56 (21.9)		
High	269	40 (14.9)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 10-4. Analysis of Malignant Skin Neoplasms (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
n	Analysis Results for Log_2 (1987 Dioxin + 1) Adjusted Relative Risk (95% C.I.)[a]	p-Value
797	1.06 (0.91,1.25)	0.447

[a] Relative risk for a twofold increase in 1987 dioxin.

A significant inverse relation between initial dioxin levels and malignant skin neoplasms was revealed in the Model 2 unadjusted analysis (Table 10-4(c): Est. RR=0.79, p=0.015). Results were nonsignificant after adjustment for covariates (Table 10-4(d): p=0.287).

The Model 3 unadjusted analysis showed significantly more Ranch Hands in the low dioxin category with malignant skin neoplasms than Comparisons (Table 10-4(e): Est. RR=1.52, p=0.023). After adjustment for covariates, the result was marginally significant (Table 10-4(f): Adj. RR=1.45, p=0.062). All other Model 3 contrasts and the Model 4 analysis results were nonsignificant (Table 10-4(e-h): p>0.10).

10.2.2.1.3 Benign Skin Neoplasms

The Model 1 unadjusted analysis showed a significant difference in the history of benign skin neoplasms between Ranch Hands and Comparisons when examined across all occupations and within the officer stratum (Table 10-5(a): Est. RR=1.31; p=0.010; Est. RR=1.42, p=0.031, respectively). Both contrasts displayed more Ranch Hands than Comparisons with benign skin neoplasms. Results were also significant in the adjusted analysis (Table 10-5(b): Adj. RR=1.31, p=0.011; Adj. RR=1.41, p=0.035, respectively). All other Model 1 contrasts were nonsignificant (Table 10-5(a,b): p≥0.22).

Table 10-5. Analysis of Benign Skin Neoplasms

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***860***	***225 (26.2)***	***1.31 (1.07,1.61)***	***0.010***
	Comparison	***1,240***	***264 (21.3)***		
Officer	Ranch Hand	336	96 (28.6)	1.42 (1.03,1.96)	0.031
	Comparison	487	107 (22.0)		
Enlisted Flyer	Ranch Hand	150	34 (22.7)	1.40 (0.82,2.40)	0.220
	Comparison	185	32 (17.3)		
Enlisted Groundcrew	Ranch Hand	374	95 (25.4)	1.21 (0.89,1.64)	0.229
	Comparison	568	125 (22.0)		

Table 10-5. Analysis of Benign Skin Neoplasms (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.31 (1.07,1.61)***	***0.011***
Officer	1.41 (1.02,1.95)	0.035
Enlisted Flyer	1.41 (0.82,2.43)	0.220
Enlisted Groundcrew	1.20 (0.88,1.63)	0.257

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	154	42 (27.3)	0.82 (0.69,0.98)	0.022
Medium	161	40 (24.8)		
High	160	27 (16.9)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
n	Analysis Results for Log_2 (Initial Dioxin) Adjusted Relative Risk (95% C.I.)[a]	p-Value
475	0.79 (0.64,0.97)	0.020

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,202	258 (21.5)		
Background RH	378	115 (30.4)	1.64 (1.26,2.13)	<0.001
Low RH	233	58 (24.9)	1.21 (0.87,1.67)	0.261
High RH	242	51 (21.1)	0.96 (0.68,1.34)	0.802
Low plus High RH	475	109 (23.0)	1.07 (0.83,1.38)	0.592

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 10-5. Analysis of Benign Skin Neoplasms (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,200		
Background RH	377	1.64 (1.25,2.15)	<0.001
Low RH	233	1.21 (0.87,1.69)	0.265
High RH	242	0.95 (0.67,1.36)	0.798
Low plus High RH	475	1.07 (0.82,1.39)	0.603

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	286	87 (30.4)	0.85 (0.77,0.95)	0.003
Medium	280	79 (28.2)		
High	287	58 (20.2)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
852	0.84 (0.74,0.95)	0.005

[a] Relative risk for a twofold increase in 1987 dioxin.

Both the unadjusted and adjusted Model 2 analyses displayed a significant inverse association between initial dioxin and benign skin neoplasms (Table 10-5(c,d): Est. RR=0.82; p=0.022; Adj. RR=0.79, p=0.020, respectively). As initial dioxin in Ranch Hands increased, benign skin neoplasms decreased.

Significant results from the Model 3 unadjusted and adjusted analyses revealed more benign skin neoplasms for Ranch Hands in the background dioxin category than for Comparisons (Table 10-5(e,f): Est. RR=1.64, p<0.001; Adj. RR=1.64, p<0.001, respectively). All other Model 3 contrasts were nonsignificant (Table 10-5(e,f): p>0.26).

Results from the Model 4 analysis of benign skin neoplasms were similar in both the unadjusted and adjusted analyses. A significant inverse association was found between 1987 dioxin and benign skin neoplasms (Table 10-5(g,h): Est. RR=0.85, p=0.003; Adj. RR=0.84, p=0.005, respectively).

10.2.2.1.4 Skin Neoplasms of Uncertain Behavior or Unspecified Nature

All results from the Model 1 through 4 analyses of skin neoplasms of uncertain behavior or unspecified nature were nonsignificant (Table 10-6(a-h): p>0.11 for each analysis).

Table 10-6. Analysis of Skin Neoplasms of Uncertain Behavior or Unspecified Nature

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***805***	***7 (0.9)***	***1.27 (0.46,3.52)***	***0.645***
	Comparison	***1,168***	***8 (0.7)***		
Officer	Ranch Hand	329	0 (0.0)	--	0.397[a]
	Comparison	480	3 (0.6)		
Enlisted Flyer	Ranch Hand	140	0 (0.0)	--	0.999[a]
	Comparison	173	1 (0.6)		
Enlisted Groundcrew	Ranch Hand	336	7 (2.1)	2.72 (0.79,9.36)	0.113
	Comparison	515	4 (0.8)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of Ranch Hands with a skin neoplasm of uncertain behavior or unspecified nature.
--: Results not presented because of the sparse number of Ranch Hands with a skin neoplasm of uncertain behavior or unspecified nature.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.18 (0.42,3.36)***	***0.755***
Officer	--	--
Enlisted Flyer	--	--
Enlisted Groundcrew	2.57 (0.73,9.10)	0.144

--: Results not presented because of the sparse number of Ranch Hands with a skin neoplasm of uncertain behavior or unspecified nature.

Note: Results are not adjusted for skin reaction to sun after repeated exposure because of the sparse number of Ranch Hands with a skin neoplasm of uncertain behavior or unspecified nature.

Table 10-6. Analysis of Skin Neoplasms of Uncertain Behavior or Unspecified Nature (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	138	1 (0.7)	0.87 (0.44,1.75)	0.696
Medium	150	3 (2.0)		
High	151	1 (0.7)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
439	0.88 (0.42,1.85)	0.732

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for occupation, skin color, eye color, skin reaction to sun after first exposure, skin reaction to sun after repeated exposure, composite skin-reaction index, and industrial chemicals exposure because of the sparse number of Ranch Hands with a skin neoplasm of uncertain behavior or unspecified nature.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,133	8 (0.7)		
Background RH	359	2 (0.6)	0.80 (0.17,3.80)	0.777
Low RH	210	3 (1.4)	2.03 (0.53,7.72)	0.300
High RH	229	2 (0.9)	1.22 (0.26,5.84)	0.800
Low plus High RH	439	5 (1.1)	1.56 (0.49,4.91)	0.449

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 10-6. Analysis of Skin Neoplasms of Uncertain Behavior or Unspecified Nature (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,131		
Background RH	358	0.92 (0.18,4.75)	0.921
Low RH	210	1.91 (0.47,7.69)	0.363
High RH	229	0.89 (0.18,4.41)	0.889
Low plus High RH	439	1.28 (0.40,4.14)	0.675

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for skin reaction to sun after repeated exposure because of the sparse number of participants with a skin neoplasm of uncertain behavior or unspecified nature.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	273	1 (0.4)	1.16 (0.72,1.86)	0.542
Medium	256	2 (0.8)		
High	269	4 (1.5)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
798	1.11 (0.69,1.81)	0.664

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for occupation, skin color, eye color, skin reaction to sun after first exposure, skin reaction to sun after repeated exposure, composite skin-reaction index, and industrial chemicals exposure because of the sparse number of Ranch Hands with a skin neoplasm of uncertain behavior or unspecified nature.

10.2.2.1.5 Basal Cell Carcinoma (All Sites Combined)

The difference in the history of any basal cell carcinoma within the enlisted flyer stratum was marginally significant and higher for Ranch Hands than for Comparisons in the Model 1 unadjusted analysis (Table 10-7(a,b): Est. RR=1.85, p=0.060). The result was significant after covariate adjustment (Table 10-7(b): Adj. RR=1.97, p=0.046). All other Model 1 contrasts were nonsignificant (Table 10-7(a,b): p>0.12).

Table 10-7. Analysis of Basal Cell Carcinoma (All Sites Combined)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***805***	***121 (15.0)***	***1.16 (0.89,1.49)***	***0.269***
	Comparison	***1,168***	***155 (13.3)***		
Officer	Ranch Hand	329	67 (20.4)	1.28 (0.89,1.83)	0.181
	Comparison	480	80 (16.7)		
Enlisted Flyer	Ranch Hand	140	26 (18.6)	1.85 (0.98,3.50)	0.060
	Comparison	173	19 (11.0)		
Enlisted Groundcrew	Ranch Hand	336	28 (8.3)	0.75 (0.46,1.20)	0.226
	Comparison	515	56 (10.9)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.21 (0.92,1.59)***	***0.169***
Officer	1.34 (0.92,1.96)	0.129
Enlisted Flyer	1.97 (1.01,3.85)	0.046
Enlisted Groundcrew	0.80 (0.49,1.30)	0.363

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	138	28 (20.3)	0.67 (0.53,0.85)	<0.001
Medium	150	27 (18.0)		
High	151	10 (6.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

Table 10-7. Analysis of Basal Cell Carcinoma (All Sites Combined) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
n	Analysis Results for Log_2 (Initial Dioxin) Adjusted Relative Risk (95% C.I.)[a]	p-Value
439	0.70 (0.53,0.94)	0.014

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,133	150 (13.2)		
Background RH	359	56 (15.6)	1.24 (0.89,1.73)	0.212
Low RH	210	42 (20.0)	1.62 (1.11,2.38)	0.012
High RH	229	23 (10.0)	0.72 (0.45,1.14)	0.160
Low plus High RH	439	65 (14.8)	1.06 (0.76,1.47)	0.727

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,131		
Background RH	358	1.16 (0.81,1.65)	0.427
Low RH	210	1.59 (1.06,2.39)	0.026
High RH	229	0.99 (0.60,1.64)	0.979
Low plus High RH	439	1.24 (0.88,1.77)	0.223

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 10-7. Analysis of Basal Cell Carcinoma (All Sites Combined) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	273	42 (15.4)	0.87 (0.76,0.99)	0.037
Medium	256	49 (19.1)		
High	269	30 (11.2)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
797	0.99 (0.83,1.18)	0.924

[a] Relative risk for a twofold increase in 1987 dioxin.

An inverse association between initial dioxin and any basal cell carcinoma was significant in both the unadjusted and adjusted Model 2 analyses (Table 10-7(c,d): Est. RR=0.67, p<0.001; Adj. RR=0.70, p=0.014, respectively). As initial dioxin in Ranch Hands increased, the percentage of participants with a basal cell carcinoma decreased.

Ranch Hands in the low dioxin category exhibited more basal cell carcinomas than did Comparisons in both the unadjusted and adjusted Model 3 analyses (Table 10-7(e,f): Est. RR=1.62, p=0.012; Adj. RR=1.59, p=0.026, respectively). All other Model 3 contrasts were nonsignificant (Table 10-7(e,f): p≥0.16).

The Model 4 unadjusted analysis revealed a significant inverse association between any basal cell carcinoma and 1987 dioxin levels (Table 10-7(g): Est. RR=0.87, p=0.037). After adjustment for covariates, the association was nonsignificant (Table 10-7(h): p=0.924).

10.2.2.1.6 Basal Cell Carcinoma (Ear, Face, Head, and Neck)

The Model 1 adjusted analysis revealed a marginally significant result within the enlisted flyer stratum, indicating more basal cell carcinomas of the ear, face, head, and neck in Ranch Hands than in Comparisons (Table 10-8(b): Adj. RR=1.83, p=0.097). All other Model 1 contrasts were nonsignificant (Table 10-8(a,b): p≥0.12).

Table 10-8. Analysis of Basal Cell Carcinoma (Ear, Face, Head, and Neck)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***805***	***93 (11.6)***	***1.14 (0.86,1.52)***	***0.370***
	Comparison	***1,168***	***120 (10.3)***		
Officer	Ranch Hand	329	49 (14.9)	1.23 (0.82,1.84)	0.328
	Comparison	480	60 (12.5)		
Enlisted Flyer	Ranch Hand	140	22 (15.7)	1.71 (0.87,3.37)	0.120
	Comparison	173	17 (9.8)		
Enlisted Groundcrew	Ranch Hand	336	22 (6.6)	0.77 (0.45,1.31)	0.334
	Comparison	515	43 (8.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.20 (0.89,1.62)***	***0.242***
Officer	1.29 (0.84,1.97)	0.244
Enlisted Flyer	1.83 (0.90,3.72)	0.097
Enlisted Groundcrew	0.84 (0.48,1.45)	0.527

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	138	21 (15.2)	0.63 (0.48,0.83)	<0.001
Medium	150	24 (16.0)		
High	151	5 (3.3)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

n	Analysis Results for Log_2 (Initial Dioxin) Adjusted Relative Risk (95% C.I.)[a]	p-Value
439	0.62 (0.44,0.87)	0.003

[a] Relative risk for a twofold increase in initial dioxin.

Table 10-8. Analysis of Basal Cell Carcinoma (Ear, Face, Head, and Neck) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,133	115 (10.2)		
Background RH	359	43 (12.0)	1.21 (0.83,1.76)	0.316
Low RH	210	33 (15.7)	1.65 (1.08,2.50)	0.020
High RH	229	17 (7.4)	0.71 (0.41,1.20)	0.199
Low plus High RH	439	50 (11.4)	1.06 (0.73,1.53)	0.762

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,131		
Background RH	358	1.19 (0.80,1.77)	0.386
Low RH	210	1.54 (0.98,2.42)	0.061
High RH	229	0.95 (0.54,1.67)	0.846
Low plus High RH	439	1.19 (0.80,1.77)	0.379

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for $\log_2$ (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	273	32 (11.7)	0.84 (0.72,0.98)	0.021
Medium	256	37 (14.5)		
High	269	24 (8.9)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 10-8. Analysis of Basal Cell Carcinoma (Ear, Face, Head, and Neck) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
797	0.89 (0.74,1.09)	0.257

[a] Relative risk for a twofold increase in 1987 dioxin.

A significant inverse relation between initial dioxin and basal cell carcinomas of the ear, face, head, and neck was found in both the Model 2 unadjusted and adjusted analyses (Table 10-8(c,d): Est. RR=0.63, p<0.001; Adj. RR=0.62, p=0.003, respectively). As initial dioxin in Ranch Hands increased, basal cell carcinomas of the ear, face, head, and neck decreased.

The Model 3 unadjusted analysis indicated more basal cell carcinomas of the ear, face, head, and neck for Ranch Hands in the low dioxin category than for Comparisons (Table 10-8(e): Est. RR=1.65, p=0.020). Results were marginally significant after adjustment for covariates (Table 10-8(f): Adj. RR=1.54, p=0.061). All other Model 3 contrasts were nonsignificant (Table 10-8 (e,f): p>0.19).

The Model 4 unadjusted analysis displayed a significant inverse relation between 1987 dioxin levels and basal cell carcinomas of the ear, face, head, and neck (Table 10-8(g): Est. RR=0.84, p=0.021). After adjustment for covariates, the result was nonsignificant (Table 10-8(h): p=0.257).

10.2.2.1.7 Basal Cell Carcinoma (Trunk)

All results from the analyses of basal cell carcinoma of the trunk from Models 1 through 3 and from the unadjusted analysis of Model 4 were nonsignificant (Table 10-9(a-g): p>0.10 for each analysis). After adjustment for covariates in Model 4, the result was significant, indicating an increase in basal cell carcinomas of the trunk as 1987 dioxin levels increased (Table 10-9(h): Adj. RR=1.51, p=0.016).

Table 10-9. Analysis of Basal Cell Carcinoma (Trunk)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***805***	***40 (5.0)***	***1.25 (0.81,1.92)***	***0.318***
	Comparison	***1,168***	***47 (4.0)***		
Officer	Ranch Hand	329	29 (8.8)	1.50 (0.88,2.57)	0.135
	Comparison	480	29 (6.0)		
Enlisted Flyer	Ranch Hand	140	6 (4.3)	2.54 (0.62,10.33)	0.194
	Comparison	173	3 (1.7)		
Enlisted Groundcrew	Ranch Hand	336	5 (1.5)	0.50 (0.18,1.40)	0.188
	Comparison	515	15 (2.9)		

Table 10-9. Analysis of Basal Cell Carcinoma (Trunk) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.24 (0.79,1.94)***	***0.357***
Officer	1.47 (0.85,2.57)	0.170
Enlisted Flyer	2.47 (0.59,10.26)	0.214
Enlisted Groundcrew	0.52 (0.19,1.48)	0.222

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	138	9 (6.5)	0.79 (0.56,1.13)	0.184
Medium	150	7 (4.7)		
High	151	6 (4.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
439	1.18 (0.75,1.86)	0.470

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for skin reaction to sun after first exposure because of the sparse number of Ranch Hands with a basal cell carcinoma on the trunk.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,133	46 (4.1)		
Background RH	359	18 (5.0)	1.28 (0.73,2.25)	0.383
Low RH	210	14 (6.7)	1.67 (0.90,3.10)	0.105
High RH	229	8 (3.5)	0.83 (0.39,1.79)	0.638
Low plus High RH	439	22 (5.0)	1.16 (0.68,1.99)	0.589

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 10-9. Analysis of Basal Cell Carcinoma (Trunk) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,131		
Background RH	358	0.99 (0.55,1.79)	0.984
Low RH	210	1.60 (0.83,3.11)	0.161
High RH	229	1.46 (0.63,3.36)	0.374
Low plus High RH	439	1.53 (0.85,2.73)	0.153

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	273	14 (5.1)	0.96 (0.77,1.19)	0.695
Medium	256	15 (5.9)		
High	269	11 (4.1)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
797	1.51 (1.07,2.13)	0.016

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for skin reaction to sun after first exposure because of the sparse number of Ranch Hands with a basal cell carcinoma on the trunk.

10.2.2.1.8 Basal Cell Carcinoma (Upper Extremities)

Results from the analysis of basal cell carcinoma of the upper extremities were nonsignificant for Models 1, 3, and 4 (Table 10-10(a-b,e-h): p>0.10 for each analysis). The unadjusted Model 2 analysis revealed a significant inverse association between initial dioxin and basal cell carcinoma of the upper extremities (Table 10-10(c): Est. RR=0.51, p=0.024). After adjustment for covariates, the association was nonsignificant (Table 10-10(d): p=0.219).

Table 10-10. Analysis of Basal Cell Carcinoma (Upper Extremities)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***805***	***21 (2.6)***	***0.80 (0.46,1.37)***	***0.405***
	Comparison	***1,168***	***38 (3.3)***		
Officer	Ranch Hand	329	17 (5.2)	1.04 (0.55,1.96)	0.915
	Comparison	480	24 (5.0)		
Enlisted Flyer	Ranch Hand	140	1 (0.7)	0.62 (0.06,6.85)	0.693
	Comparison	173	2 (1.2)		
Enlisted Groundcrew	Ranch Hand	336	3 (0.9)	0.38 (0.11,1.35)	0.134
	Comparison	515	12 (2.3)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.76 (0.44,1.34)***	***0.340***
Officer	0.98 (0.51,1.89)	0.947
Enlisted Flyer	0.56 (0.05,6.30)	0.635
Enlisted Groundcrew	0.38 (0.11,1.37)	0.139

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	138	5 (3.6)	0.51 (0.26,0.99)	0.024
Medium	150	5 (3.3)		
High	151	0 (0.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

n	Analysis Results for Log_2 (Initial Dioxin) Adjusted Relative Risk (95% C.I.)[a]	p-Value
439	0.56 (0.21,1.51)	0.219

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for eye color, ionizing radiation exposure, and skin reaction to sun after first exposure because of the sparse number of Ranch Hands with a basal cell carcinoma on the upper extremities.

Table 10-10. Analysis of Basal Cell Carcinoma (Upper Extremities) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,133	37 (3.3)		
Background RH	359	11 (3.1)	0.99 (0.50,1.97)	0.981
Low RH	210	7 (3.3)	1.00 (0.44,2.27)	0.993
High RH	229	3 (1.3)	0.37 (0.11,1.22)	0.102
Low plus High RH	439	10 (2.3)	0.60 (0.28,1.29)	0.188

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,131		
Background RH	358	0.74 (0.36,1.52)	0.416
Low RH	210	0.93 (0.39,2.21)	0.876
High RH	229	0.64 (0.18,2.23)	0.484
Low plus High RH	439	0.77 (0.34,1.71)	0.518

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	273	9 (3.3)	0.77 (0.56,1.07)	0.107
Medium	256	8 (3.1)		
High	269	4 (1.5)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 10-10. Analysis of Basal Cell Carcinoma (Upper Extremities) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
n	Analysis Results for Log_2 (1987 Dioxin + 1) Adjusted Relative Risk (95% C.I.)[a]	p-Value
797	1.00 (0.63,1.57)	0.987

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for eye color and skin reaction to sun after first exposure because of the sparse number of Ranch Hands with a basal cell carcinoma on the upper extremities.

10.2.2.1.9 Basal Cell Carcinoma (Lower Extremities)

All results from Models 1 through 4 of the analysis of basal cell carcinoma of the lower extremities were nonsignificant (Table 10-11(a-h): p>0.32 for each analysis).

Table 10-11. Analysis of Basal Cell Carcinoma (Lower Extremities)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***805***	***5 (0.6)***	***1.45 (0.42,5.04)***	***0.556***
	Comparison	***1,168***	***5 (0.4)***		
Officer	Ranch Hand	329	4 (1.2)	1.96 (0.44,8.80)	0.381
	Comparison	480	3 (0.6)		
Enlisted Flyer	Ranch Hand	140	0 (0.0)	--	--
	Comparison	173	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	336	1 (0.3)	0.77 (0.07,8.48)	0.828
	Comparison	515	2 (0.4)		

--: Results not presented because of the sparse number of participants with a basal cell carcinoma on the lower extremities.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.38 (0.39,4.85)***	***0.616***
Officer	1.83 (0.40,8.33)	0.436
Enlisted Flyer	--	--
Enlisted Groundcrew	0.78 (0.07,8.71)	0.839

--: Results not presented because of the sparse number of participants with a basal cell carcinoma on the lower extremities.

Note: Results are not adjusted for skin reaction to sun after first exposure or skin reaction to sun after repeated exposure because of the sparse number of participants with a basal cell carcinoma on the lower extremities. Results for all occupations combined also are not adjusted for occupation because of the sparse number of participants with a basal cell carcinoma on the lower extremities.

Table 10-11. Analysis of Basal Cell Carcinoma (Lower Extremities) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	138	1 (0.7)	1.09 (0.39,3.02)	0.867
Medium	150	0 (0.0)		
High	151	1 (0.7)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
439	1.46 (0.50,4.26)	0.511

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for occupation, skin color, hair color, eye color, skin reaction to sun after first exposure, skin reaction to sun after repeated exposure, composite skin-reaction index, and ionizing radiation exposure because of the sparse number of Ranch Hands with a basal cell carcinoma on the lower extremities.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,133	5 (0.4)		
Background RH	359	3 (0.8)	2.07 (0.48,8.80)	0.327
Low RH	210	1 (0.5)	1.04 (0.12,8.97)	0.972
High RH	229	1 (0.4)	0.91 (0.10,7.91)	0.932
Low plus High RH	439	2 (0.5)	0.97 (0.19,5.06)	0.971

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 10-11. Analysis of Basal Cell Carcinoma (Lower Extremities) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,131		
Background RH	358	1.89 (0.43,8.34)	0.398
Low RH	210	0.90 (0.10,8.17)	0.928
High RH	229	1.03 (0.12,9.27)	0.976
Low plus High RH	439	0.97 (0.18,5.16)	0.971

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for occupation and skin reaction to sun after first exposure because of the sparse number of participants with a basal cell carcinoma on the lower extremities.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	273	3 (1.1)	0.85 (0.45,1.59)	0.597
Medium	256	1 (0.4)		
High	269	1 (0.4)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
797	0.91 (0.42,1.98)	0.803

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for occupation, skin reaction to sun after first exposure, and skin reaction to sun after repeated exposure because of the sparse number of Ranch Hands with a basal cell carcinoma on the lower extremities.

10.2.2.1.10 Squamous Cell Carcinoma

All results were nonsignificant from the Model 1 through 4 analyses of squamous cell carcinoma (Table 10-12(a-h): p>0.13 for each analysis).

Table 10-12. Analysis of Squamous Cell Carcinoma

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***805***	***20 (2.5)***	***1.33 (0.72,2.45)***	***0.367***
	Comparison	***1,168***	***22 (1.9)***		
Officer	Ranch Hand	329	11 (3.3)	1.00 (0.46,2.19)	0.994
	Comparison	480	16 (3.3)		
Enlisted Flyer	Ranch Hand	140	3 (2.1)	1.87 (0.31,11.36)	0.495
	Comparison	173	2 (1.2)		
Enlisted Groundcrew	Ranch Hand	336	6 (1.8)	2.32 (0.65,8.29)	0.194
	Comparison	515	4 (0.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.46 (0.77,2.78)***	***0.250***
Officer	1.10 (0.49,2.49)	0.813
Enlisted Flyer	1.86 (0.29,11.86)	0.514
Enlisted Groundcrew	2.67 (0.73,9.76)	0.139

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	138	3 (2.2)	0.95 (0.58,1.55)	0.821
Medium	150	3 (2.0)		
High	151	4 (2.7)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
n	Analysis Results for Log_2 (Initial Dioxin) Adjusted Relative Risk (95% C.I.)[a]	p-Value
439	0.98 (0.52,1.85)	0.944

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for skin reaction to sun after repeated exposure because of the sparse number of Ranch Hands with a squamous cell carcinoma.

Table 10-12. Analysis of Squamous Cell Carcinoma (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,133	20 (1.8)		
Background RH	359	10 (2.8)	1.69 (0.78,3.66)	0.187
Low RH	210	6 (2.9)	1.60 (0.63,4.04)	0.320
High RH	229	4 (1.8)	0.94 (0.32,2.78)	0.907
Low plus High RH	439	10 (2.3)	1.21 (0.55,2.66)	0.634

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,131		
Background RH	358	1.53 (0.68,3.45)	0.306
Low RH	210	1.52 (0.56,4.10)	0.408
High RH	229	1.74 (0.53,5.69)	0.363
Low plus High RH	439	1.63 (0.69,3.82)	0.262

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	273	8 (2.9)	0.95 (0.70,1.29)	0.744
Medium	256	6 (2.3)		
High	269	6 (2.2)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 10-12. Analysis of Squamous Cell Carcinoma (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
797	1.07 (0.70,1.63)	0.749

[a] Relative risk for a twofold increase in 1987 dioxin.

10.2.2.1.11 Nonmelanoma

Both the unadjusted and adjusted Model 1 analyses of nonmelanoma revealed a significant difference between Ranch Hand and Comparison enlisted flyers (Table 10-13(a,b): Est. RR=1.89, p=0.042; Adj. RR=2.00, p=0.035, respectively). Nonmelanoma was higher in Ranch Hands than in Comparisons. All other Model 1 contrasts were nonsignificant (Table 10-13(a,b): p>0.14).

The Model 2 unadjusted analysis revealed a significant inverse association between initial dioxin and nonmelanoma (Table 10-13(c): Est. RR=0.73, p=0.003). After adjustment for covariates, the association was marginally significant (Table 10-13(d): Adj. RR=0.79, p=0.075).

The Model 3 unadjusted analysis revealed that Ranch Hands in the low dioxin category had a greater history of nonmelanoma than Comparisons (Table 10-13(e): Est. RR=1.49, p=0.034). The result was marginally significant after adjustment for covariates (Table 10-13(f): Adj. RR=1.43, p=0.081). All other Model 3 contrasts were nonsignificant (Table 10-13(e,f): p>0.20).

Table 10-13. Analysis of Nonmelanoma

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***805***	***134 (16.7)***	***1.13 (0.88,1.44)***	***0.345***
	Comparison	***1,168***	***176 (15.1)***		
Officer	Ranch Hand	329	73 (22.2)	1.25 (0.89,1.77)	0.203
	Comparison	480	89 (18.5)		
Enlisted Flyer	Ranch Hand	140	29 (20.7)	1.89 (1.02,3.49)	0.042
	Comparison	173	21 (12.1)		
Enlisted Groundcrew	Ranch Hand	336	32 (9.5)	0.72 (0.46,1.12)	0.143
	Comparison	515	66 (12.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.18 (0.91,1.53)***	***0.219***
Officer	1.31 (0.91,1.90)	0.144
Enlisted Flyer	2.00 (1.05,3.81)	0.035
Enlisted Groundcrew	0.76 (0.48,1.22)	0.258

Table 10-13. Analysis of Nonmelanoma (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	138	29 (21.0)	0.73 (0.59,0.90)	0.003
Medium	150	29 (19.3)		
High	151	14 (9.3)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
439	0.79 (0.60,1.03)	0.075

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,133	169 (14.9)		
Background RH	359	62 (17.3)	1.23 (0.89,1.70)	0.203
Low RH	210	44 (21.0)	1.49 (1.03,2.16)	0.034
High RH	229	28 (12.2)	0.77 (0.50,1.18)	0.231
Low plus High RH	439	72 (16.4)	1.06 (0.78,1.44)	0.729

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 10-13. Analysis of Nonmelanoma (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,131		
Background RH	358	1.16 (0.82,1.64)	0.398
Low RH	210	1.43 (0.96,2.13)	0.081
High RH	229	1.06 (0.67,1.69)	0.803
Low plus High RH	439	1.22 (0.88,1.71)	0.235

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	273	46 (16.9)	0.89 (0.78,1.01)	0.074
Medium	256	52 (20.3)		
High	269	36 (13.4)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
797	1.02 (0.86,1.21)	0.786

[a] Relative risk for a twofold increase in 1987 dioxin.

A marginally significant association between 1987 dioxin levels and nonmelanoma was revealed from the Model 4 unadjusted analysis (Table 10-13(g): Est. RR=0.89, p=0.074). After adjustment for covariates, the result was nonsignificant (Table 10-13(h): p=0.786).

10.2.2.1.12 Melanoma

All analyses of melanoma in Models 1, 2, and 4 were nonsignificant (Table 10-14(a-d,g-h): p>0.11 for each analysis). All contrasts from the unadjusted analysis of Model 3 were nonsignificant (Table 10-14(e): p>0.11 for each contrast). After adjustment for covariates, a marginally significant difference was found between Ranch Hands in the low plus high dioxin category and Comparisons (Table 10-14(f): Adj. RR=2.44, p=0.062). Melanoma was higher for Ranch Hands than for Comparisons. All other adjusted Model 3 contrasts were nonsignificant (Table 10-14(f): p>0.12).

Table 10-14. Analysis of Melanoma

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***805***	***16 (2.0)***	***1.80 (0.86,3.77)***	***0.117***
	Comparison	***1,168***	***13 (1.1)***		
Officer	Ranch Hand	329	9 (2.7)	1.90 (0.70,5.16)	0.207
	Comparison	480	7 (1.5)		
Enlisted Flyer	Ranch Hand	140	0 (0.0)	--	0.999[a]
	Comparison	173	1 (0.6)		
Enlisted Groundcrew	Ranch Hand	336	7 (2.1)	2.17 (0.68,6.90)	0.189
	Comparison	515	5 (1.0)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of Ranch Hands with a melanoma.
--: Results not presented because of the sparse number of Ranch Hands with a melanoma.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.78 (0.83,3.79)***	***0.136***
Officer	1.92 (0.69,5.30)	0.211
Enlisted Flyer	--	--
Enlisted Groundcrew	2.01 (0.62,6.50)	0.246

--: Results not presented because of the sparse number of Ranch Hands with a melanoma.

Note: Results are not adjusted for skin reaction to sun after first exposure because of the sparse number of Ranch Hands with a melanoma.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	138	4 (2.9)	1.12 (0.69,1.80)	0.660
Medium	150	1 (0.7)		
High	151	4 (2.7)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

Table 10-14. Analysis of Melanoma (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
n	Analysis Results for Log_2 (Initial Dioxin) Adjusted Relative Risk (95% C.I.)[a]	p-Value
439	1.28 (0.76,2.16)	0.366

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for occupation, skin color, skin reaction to sun after first exposure, and skin reaction to sun after repeated exposure because of the sparse number of Ranch Hands with a melanoma.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,133	12 (1.1)		
Background RH	359	7 (2.0)	1.76 (0.68,4.54)	0.240
Low RH	210	5 (2.4)	2.32 (0.81,6.68)	0.117
High RH	229	4 (1.8)	1.74 (0.55,5.49)	0.341
Low plus High RH	439	9 (2.1)	2.00 (0.83,4.83)	0.122

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,131		
Background RH	358	1.56 (0.59,4.16)	0.373
Low RH	210	2.17 (0.73,6.48)	0.164
High RH	229	2.71 (0.76,9.67)	0.124
Low plus High RH	439	2.44 (0.96,6.23)	0.062

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for skin reaction to sun after first exposure because of the sparse number of participants with a melanoma.

Table 10-14. Analysis of Melanoma (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	273	5 (1.8)	1.05 (0.76,1.46)	0.761
Medium	256	7 (2.7)		
High	269	4 (1.5)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
797	1.18 (0.81,1.71)	0.399

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for occupation and skin reaction to sun after repeated exposure because of the sparse number of Ranch Hands with a melanoma.

10.2.2.1.13 Systemic Neoplasms (All Sites Combined)

Results from the analyses of a history of all systemic neoplasms in Models 1, 2, and 4 were nonsignificant (Table 10-15(a-d,g-h): p>0.12 for each analysis). In the unadjusted analysis of Model 3, a marginally significant difference in the percentage of participants with any systemic neoplasm was found between Ranch Hands in the low dioxin category and Comparisons (Table 10-15(e): Est. RR=1.31, p=0.072). The occurrence of any systemic neoplasm was higher for Ranch Hands in the low dioxin category than for Comparisons. After adjustment for covariates, the contrast was nonsignificant (Table 10-15(f): p=0.927). The contrast of Ranch Hands in the background dioxin category and Comparisons was marginally significant in the adjusted Model 3 analysis (Table 10-15(f): Adj. RR=0.76, p=0.076). A greater percentage of Comparisons than Ranch Hands in the background dioxin category had a systemic neoplasm. All other Model 3 contrasts were nonsignificant (Table 10-15(e,f): p>0.25).

Table 10-15. Analysis of Systemic Neoplasms (All Sites Combined)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***855***	***267 (31.2)***	***1.07 (0.89,1.29)***	***0.482***
	Comparison	***1,242***	***370 (29.8)***		
Officer	Ranch Hand	332	110 (33.1)	0.95 (0.70,1.27)	0.716
	Comparison	489	168 (34.4)		
Enlisted Flyer	Ranch Hand	147	49 (33.3)	1.20 (0.75,1.91)	0.443
	Comparison	187	55 (29.4)		
Enlisted Groundcrew	Ranch Hand	376	108 (28.7)	1.15 (0.86,1.54)	0.352
	Comparison	566	147 (26.0)		

Table 10-15. Analysis of Systemic Neoplasms (All Sites Combined) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.88 (0.70,1.12)***	***0.307***
Officer	0.77 (0.56,1.07)	0.125
Enlisted Flyer	0.98 (0.60,1.61)	0.937
Enlisted Groundcrew	0.98 (0.70,1.36)	0.888

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	155	57 (36.8)	0.93 (0.80,1.07)	0.308
Medium	160	52 (32.5)		
High	157	46 (29.3)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
n	Analysis Results for Log_2 (Initial Dioxin) Adjusted Relative Risk (95% C.I.)[a]	p-Value
469	1.00 (0.84,1.20)	0.980

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,204	358 (29.7)		
Background RH	376	109 (29.0)	0.98 (0.76,1.26)	0.864
Low RH	232	83 (35.8)	1.31 (0.98,1.76)	0.072
High RH	240	72 (30.0)	1.00 (0.74,1.36)	0.995
Low plus High RH	472	155 (32.8)	1.14 (0.91,1.44)	0.253

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 10-15. Analysis of Systemic Neoplasms (All Sites Combined) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,202		
Background RH	373	0.76 (0.57,1.03)	0.076
Low RH	230	0.98 (0.70,1.38)	0.927
High RH	239	0.95 (0.67,1.36)	0.794
Low plus High RH	469	0.97 (0.73,1.28)	0.823

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	284	83 (29.2)	1.02 (0.92,1.12)	0.734
Medium	281	94 (33.5)		
High	283	87 (30.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
842	1.05 (0.93,1.18)	0.399

[a] Relative risk for a twofold increase in 1987 dioxin.

10.2.2.1.14 Malignant Systemic Neoplasms

The unadjusted Model 1 analysis within the enlisted flyer stratum revealed significantly more Ranch Hands than Comparisons with a malignant systemic neoplasm (Table 10-16(a): Est. RR=2.20, p=0.049). After adjustment for covariates the contrast was nonsignificant (Table 10-16(b): p=0.132). All other Model 1 contrasts were nonsignificant (Table 10-16(a,b): p>0.11).

Table 10-16. Analysis of Malignant Systemic Neoplasms

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***861***	***67 (7.8)***	***1.32 (0.94,1.86)***	***0.112***
	Comparison	***1,249***	***75 (6.0)***		
Officer	Ranch Hand	335	32 (9.6)	1.23 (0.76,2.01)	0.403
	Comparison	494	39 (7.9)		
Enlisted Flyer	Ranch Hand	149	18 (12.1)	2.20 (1.00,4.81)	0.049
	Comparison	187	11 (5.9)		
Enlisted Groundcrew	Ranch Hand	377	17 (4.5)	1.03 (0.55,1.93)	0.937
	Comparison	568	25 (4.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.12 (0.74,1.70)***	***0.592***
Officer	1.09 (0.63,1.88)	0.766
Enlisted Flyer	1.91 (0.82,4.43)	0.132
Enlisted Groundcrew	0.82 (0.41,1.67)	0.589

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	156	19 (12.2)	0.62 (0.46,0.84)	0.001
Medium	161	20 (12.4)		
High	159	6 (3.8)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
n	Analysis Results for Log_2 (Initial Dioxin) Adjusted Relative Risk (95% C.I.)[a]	p-Value
472	0.82 (0.57,1.18)	0.272

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

Table 10-16. Analysis of Malignant Systemic Neoplasms (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	**n**	**Number (%) Yes**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,211	73 (6.0)		
Background RH	378	21 (5.6)	0.91 (0.55,1.51)	0.727
Low RH	234	34 (14.5)	2.65 (1.72,4.09)	<0.001
High RH	242	11 (4.6)	0.74 (0.39,1.43)	0.374
Low plus High RH	476	45 (9.5)	1.39 (0.91,2.13)	0.132

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Comparison	1,209		
Background RH	375	0.73 (0.42,1.29)	0.279
Low RH	232	1.94 (1.16,3.24)	0.012
High RH	240	0.86 (0.41,1.78)	0.680
Low plus High RH	472	1.28 (0.77,2.13)	0.345

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			**Analysis Results for $\log_2$ (1987 Dioxin + 1)**	
1987 Dioxin	**n**	**Number (%) Yes**	**Estimated Relative Risk (95% C.I.)[a]**	**p-Value**
Low	286	15 (5.2)	0.96 (0.81,1.14)	0.641
Medium	282	32 (11.4)		
High	286	19 (6.6)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 10-16. Analysis of Malignant Systemic Neoplasms (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
847	1.06 (0.84,1.34)	0.599

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

The unadjusted analysis of malignant systemic neoplasms revealed a significant inverse relation with initial dioxin (Table 10-16(a): Est. RR=0.62, p=0.001). The association was nonsignificant after adjustment for covariates (Table 10-16(d): p=0.272).

The Model 3 contrast between Ranch Hands in the low dioxin category and Comparisons was significant in both the unadjusted and adjusted analyses. A greater percentage of participants with malignant systemic neoplasms was observed in Ranch Hands than in Comparisons (Table 10-16(e,f): Est. RR=2.65, p<0.001; Adj. RR=1.94, p=0.012, respectively). All other Model 3 contrasts, as well as the Model 4 analyses, were nonsignificant (Table 10-16(e-h): p>0.13 for all remaining analyses).

10.2.2.1.15 Benign Systemic Neoplasms

Results from each of the analyses of benign systemic neoplasms in Models 1 through 4 were nonsignificant (Table 10-17(a-h): p>0.15 for each analysis).

Table 10-17. Analysis of Benign Systemic Neoplasms

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***855***	***217 (25.4)***	***1.07 (0.88,1.31)***	***0.495***
	Comparison	***1,242***	***299 (24.1)***		
Officer	Ranch Hand	332	82 (24.7)	0.91 (0.66,1.25)	0.545
	Comparison	489	130 (26.6)		
Enlisted Flyer	Ranch Hand	147	40 (27.2)	1.11 (0.68,1.82)	0.668
	Comparison	187	47 (25.1)		
Enlisted Groundcrew	Ranch Hand	376	95 (25.3)	1.23 (0.91,1.67)	0.186
	Comparison	566	122 (21.6)		

Table 10-17. Analysis of Benign Systemic Neoplasms (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.93 (0.73,1.19)***	***0.574***
Officer	0.78 (0.55,1.10)	0.155
Enlisted Flyer	0.95 (0.56,1.59)	0.831
Enlisted Groundcrew	1.11 (0.79,1.57)	0.548

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	155	43 (27.7)	1.03 (0.88,1.20)	0.718
Medium	160	37 (23.1)		
High	157	41 (26.1)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
n	Analysis Results for Log_2 (Initial Dioxin) Adjusted Relative Risk (95% C.I.)[a]	p-Value
469	0.99 (0.82,1.19)	0.903

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,204	289 (24.0)		
Background RH	376	93 (24.7)	1.05 (0.80,1.38)	0.710
Low RH	232	58 (25.0)	1.05 (0.76,1.46)	0.760
High RH	240	63 (26.3)	1.12 (0.81,1.53)	0.500
Low plus High RH	472	121 (25.6)	1.08 (0.85,1.39)	0.521

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 10-17. Analysis of Benign Systemic Neoplasms (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,202		
Background RH	373	0.89 (0.66,1.22)	0.479
Low RH	230	0.86 (0.60,1.23)	0.400
High RH	239	1.00 (0.69,1.45)	0.996
Low plus High RH	469	0.93 (0.69,1.24)	0.613

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	284	70 (24.7)	1.03 (0.93,1.14)	0.582
Medium	281	72 (25.6)		
High	283	72 (25.4)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
842	1.01 (0.89,1.14)	0.905

[a] Relative risk for a twofold increase in 1987 dioxin.

10.2.2.1.16 Systemic Neoplasms of Uncertain Behavior or Unspecified Nature

Results from each of the analyses of systemic neoplasms of uncertain behavior or unspecified nature from Models 1 through 4 were nonsignificant (Table 10-18(a-h): p>0.18 for each analysis).

Table 10-18. Analysis of Systemic Neoplasms of Uncertain Behavior or Unspecified Nature

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***861***	***16 (1.9)***	***0.93 (0.49,1.75)***	***0.814***
	Comparison	***1,249***	***25 (2.0)***		
Officer	Ranch Hand	335	11 (3.3)	1.26 (0.56,2.84)	0.583
	Comparison	494	13 (2.6)		
Enlisted Flyer	Ranch Hand	149	1 (0.7)	0.63 (0.06,6.96)	0.702
	Comparison	187	2 (1.1)		
Enlisted Groundcrew	Ranch Hand	377	4 (1.1)	0.60 (0.19,1.92)	0.388
	Comparison	568	10 (1.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.71 (0.34,1.47)***	***0.355***
Officer	0.96 (0.40,2.31)	0.925
Enlisted Flyer	0.45 (0.04,5.19)	0.523
Enlisted Groundcrew	0.44 (0.13,1.50)	0.190

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	156	5 (3.2)	0.84 (0.49,1.47)	0.534
Medium	161	1 (0.6)		
High	159	2 (1.3)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

n	Analysis Results for Log_2 (Initial Dioxin) Adjusted Relative Risk (95% C.I.)[a]	p-Value
472	1.16 (0.58,2.31)	0.678

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

Table 10-18. Analysis of Systemic Neoplasms of Uncertain Behavior or Unspecified Nature (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	25 (2.1)		
Background RH	378	8 (2.1)	1.08 (0.48,2.44)	0.845
Low RH	234	6 (2.6)	1.23 (0.50,3.03)	0.657
High RH	242	2 (0.8)	0.38 (0.09,1.61)	0.187
Low plus High RH	476	8 (1.7)	0.67 (0.27,1.67)	0.392

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,209		
Background RH	375	0.72 (0.30,1.76)	0.475
Low RH	232	0.85 (0.32,2.26)	0.744
High RH	240	0.40 (0.09,1.89)	0.250
Low plus High RH	472	0.58 (0.22,1.58)	0.288

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	286	8 (2.8)	0.84 (0.59,1.20)	0.329
Medium	282	5 (1.8)		
High	286	3 (1.1)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 10-18. Analysis of Systemic Neoplasms of Uncertain Behavior or Unspecified Nature (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
847	1.07 (0.67,1.72)	0.767

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

10.2.2.1.17 Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck)

Results from each of the analyses of malignant systemic neoplasms of the eye, ear, face, head, and neck in Models 1, 3, and 4 were nonsignificant (Table 10-19(a-b,e-h): p>0.13 for each analysis). The unadjusted analysis of Model 2 revealed a marginally significant association between initial dioxin and malignant systemic neoplasms of the eye, ear, face, head, and neck (Table 10-19(c): Est. RR=0.50, p=0.081). After adjustment for covariates, the Model 2 result was nonsignificant (Table 10-19(d): p=0.666).

Table 10-19. Analysis of Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***861***	***9 (1.1)***	***1.09 (0.46,2.60)***	***0.848***
	Comparison	***1,249***	***12 (1.0)***		
Officer	Ranch Hand	335	6 (1.8)	2.23 (0.63,7.98)	0.216
	Comparison	494	4 (0.8)		
Enlisted Flyer	Ranch Hand	149	1 (0.7)	0.41 (0.04,4.03)	0.448
	Comparison	187	3 (1.6)		
Enlisted Groundcrew	Ranch Hand	377	2 (0.5)	0.60 (0.12,3.11)	0.543
	Comparison	568	5 (0.9)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.98 (0.35,2.75)***	***0.974***
Officer	2.07 (0.53,8.16)	0.298
Enlisted Flyer	0.38 (0.04,4.02)	0.424
Enlisted Groundcrew	0.49 (0.08,2.87)	0.429

Table 10-19. Analysis of Malignant Systemic Neoplasms (Eye, Ear, Face, Head and Neck) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	156	4 (2.6)	0.50 (0.20,1.23)	0.081
Medium	161	1 (0.6)		
High	159	1 (0.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
472	0.79 (0.27,2.33)	0.666

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the eye, ear, face, head, and neck. Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	12 (1.0)		
Background RH	378	3 (0.8)	0.72 (0.20,2.58)	0.612
Low RH	234	5 (2.1)	2.24 (0.78,6.43)	0.134
High RH	242	1 (0.4)	0.46 (0.06,3.53)	0.451
Low plus High RH	476	6 (1.3)	1.00 (0.29,3.41)	0.995

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 10-19. Analysis of Malignant Systemic Neoplasms (Eye, Ear, Face, Head and Neck) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,209		
Background RH	375	0.64 (0.16,2.59)	0.533
Low RH	232	1.94 (0.58,6.44)	0.281
High RH	240	0.49 (0.06,4.31)	0.520
Low plus High RH	472	0.96 (0.24,3.82)	0.956

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	286	2 (0.7)	0.85 (0.53,1.36)	0.494
Medium	282	5 (1.8)		
High	286	2 (0.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
n	Analysis Results for Log_2 (1987 Dioxin + 1) Adjusted Relative Risk (95% C.I.)[a]	p-Value
847	1.04 (0.57,1.91)	0.897

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the eye, ear, face, head, and neck. Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

10.2.2.1.18 Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx)

Results from each of the analyses of malignant systemic neoplasms of the oral cavity, pharynx, and larynx from Models 1 through 4 were nonsignificant (Table 10-20(a-h): p>0.29 for each analysis).

Table 10-20. Analysis of Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*861*	*4 (0.5)*	*0.83 (0.24,2.84)*	*0.762*
	Comparison	*1,249*	*7 (0.6)*		
Officer	Ranch Hand	335	2 (0.6)	1.48 (0.21,10.54)	0.697
	Comparison	494	2 (0.4)		
Enlisted Flyer	Ranch Hand	149	1 (0.7)	0.63 (0.06,6.96)	0.702
	Comparison	187	2 (1.1)		
Enlisted Groundcrew	Ranch Hand	377	1 (0.3)	0.50 (0.05,4.83)	0.550
	Comparison	568	3 (0.5)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	*0.63 (0.16,2.44)*	*0.501*
Officer	1.35 (0.17,10.61)	0.777
Enlisted Flyer	0.52 (0.04,6.28)	0.603
Enlisted Groundcrew	0.31 (0.03,3.40)	0.336

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	156	1 (0.6)	0.97 (0.39,2.41)	0.953
Medium	161	1 (0.6)		
High	159	1 (0.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

n	Analysis Results for Log_2 (Initial Dioxin) Adjusted Relative Risk (95% C.I.)[a]	p-Value
472	1.15 (0.34,3.88)	0.822

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the oral cavity, pharynx, and larynx. Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

Table 10-20. Analysis of Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	7 (0.6)		
Background RH	378	1 (0.3)	0.43 (0.05,3.52)	0.431
Low RH	234	2 (0.9)	1.51 (0.31,7.30)	0.612
High RH	242	1 (0.4)	0.75 (0.09,6.18)	0.791
Low plus High RH	476	3 (0.6)	1.06 (0.25,4.39)	0.938

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,209		
Background RH	375	0.39 (0.04,3.56)	0.401
Low RH	232	1.01 (0.18,5.59)	0.987
High RH	240	0.56 (0.06,5.33)	0.614
Low plus High RH	472	0.75 (0.16,3.59)	0.719

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	286	0 (0.0)	1.23 (0.66,2.29)	0.526
Medium	282	2 (0.7)		
High	286	2 (0.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 10-20. Analysis of Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
n	Analysis Results for Log_2 (1987 Dioxin + 1) Adjusted Relative Risk (95% C.I.)[a]	p-Value
847	1.60 (0.65,3.97)	0.296

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the oral cavity, pharynx, and larynx. Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

10.2.2.1.19 Malignant Systemic Neoplasms (Esophagus)

Because of the absence of malignant systemic neoplasms of the esophagus in Ranch Hands, statistical analysis was not performed. A malignant systemic neoplasm of the esophagus was observed in two Comparisons. One Comparison was a non-Black enlisted flyer, and the other Comparison was a non-Black enlisted groundcrew.

10.2.2.1.20 Malignant Systemic Neoplasms (Brain)

Because of the presence of a malignant systemic neoplasm of the brain in only one Ranch Hand, statistical analysis was not performed. This participant was a non-Black officer.

10.2.2.1.21 Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum)

A sparse number of participants exhibited a malignant systemic neoplasm of the thymus, heart, or mediastinum, which limited the analyses. The unadjusted contrasts analyzed from Model 1 were nonsignificant (Table 10-21(a): $p>0.32$ for each contrast). Model 2 analysis was not performed because no Ranch Hands with a malignant neoplasm of the thymus, heart, or mediastinum had an initial dioxin estimate. The Model 3 unadjusted analysis revealed a marginally significant difference between Ranch Hands in the background dioxin category and Comparisons (Table 10-21(e): $p=0.089$). Two Ranch Hands in the background category had a malignant systemic neoplasm of the thymus, heart, or mediastinum (0.5%), contrasted with zero Comparisons. The Model 4 unadjusted and adjusted analyses showed a significant inverse association between 1987 dioxin levels and a malignant systemic neoplasm of the thymus, heart, or mediastinum (Table 10-21(g,h): Est. RR=0.33; $p=0.038$; Adj. RR=0.31, $p=0.017$, respectively). As 1987 dioxin levels increased, the percentage of Ranch Hands with a malignant systemic neoplasm of the thymus, heart, or mediastinum decreased.

Table 10-21. Analysis of Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***861***	***2 (0.2)***	--	***0.325***[a]
	Comparison	***1,249***	***0 (0.0)***		
Officer	Ranch Hand	335	1 (0.3)	--	0.845[a]
	Comparison	494	0 (0.0)		
Enlisted Flyer	Ranch Hand	149	0 (0.0)	--	--
	Comparison	187	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	377	1 (0.3)	--	0.836[a]
	Comparison	568	0 (0.0)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a malignant systemic neoplasm of the thymus, heart, and mediastinum.
--: Results not presented because of the sparse number of participants with a malignant systemic neoplasm of the thymus, heart, and mediastinum.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	--	--
Officer	--	--
Enlisted Flyer	--	--
Enlisted Groundcrew	--	--

--: Results not presented because of the sparse number of participants with a malignant systemic neoplasm of the thymus, heart, and mediastinum.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)	p-Value
Low	156	0 (0.0)	--	--
Medium	161	0 (0.0)		
High	159	0 (0.0)		

--: Results not presented because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the thymus, heart, and mediastinum.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

Table 10-21. Analysis of Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)	p-Value
--	--	--

--: Results not presented because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the thymus, heart, and mediastinum.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
Comparison	1,211	0 (0.0)		
Background RH	378	2 (0.5)	--	0.089[a]
Low RH	234	0 (0.0)	--	--
High RH	242	0 (0.0)	--	--
Low plus High RH	476	0 (0.0)	--	--

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a malignant systemic neoplasm of the thymus, heart, and mediastinum.
--: Results not presented because of the sparse number of participants with a malignant systemic neoplasm of the thymus, heart, and mediastinum.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
Comparison	--		
Background RH	--	--	--
Low RH	--	--	--
High RH	--	--	--
Low plus High RH	--	--	--

--: Results not presented because of the sparse number of participants with a malignant systemic neoplasm of the thymus, heart, and mediastinum.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 10-21. Analysis of Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	286	2 (0.7)	0.33 (0.12,0.92)	0.038
Medium	282	0 (0.0)		
High	286	0 (0.0)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
847	0.31 (0.09,1.04)	0.017

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race and occupation because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the thymus, heart, and mediastinum. Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

10.2.2.1.22 Malignant Systemic Neoplasms (Thyroid Gland)

Because of the sparse number of participants with a history of a malignant systemic neoplasm of the thyroid gland, analysis was limited. The Model 1 contrasts revealed nonsignificant differences between Ranch Hands and Comparisons (Table 10-22(a,b): p>0.37 for each).

Table 10-22. Analysis of Malignant Systemic Neoplasms (Thyroid Gland)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***861***	***2 (0.2)***	***1.45 (0.20,10.33)***	***0.710***
	Comparison	***1,249***	***2 (0.2)***		
Officer	Ranch Hand	335	2 (0.6)	2.96 (0.27,32.79)	0.376
	Comparison	494	1 (0.2)		
Enlisted Flyer	Ranch Hand	149	0 (0.0)	--	--
	Comparison	187	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	377	0 (0.0)	--	0.999[a]
	Comparison	568	1 (0.2)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a malignant systemic neoplasm of the thyroid gland.
--: Results not presented because of the sparse number of participants with a malignant systemic neoplasm of the thyroid gland.

Table 10-22. Analysis of Malignant Systemic Neoplasms (Thyroid Gland) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.46 (0.20,10.39)***	***0.708***
Officer	3.08 (0.28,34.40)	0.362
Enlisted Flyer	--	--
Enlisted Groundcrew	--	--

--: Results not presented because of the sparse number of participants with a malignant systemic neoplasm of the thyroid gland.

Note: Results are not adjusted for race and ionizing radiation exposure because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the thyroid gland. Results for all occupations combined also are not adjusted for occupation because of the sparse number of participants with a malignant systemic neoplasm of the thyroid gland. Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	156	2 (1.3)	0.12 (0.01,2.59)	0.046
Medium	161	0 (0.0)		
High	159	0 (0.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
473	0.12 (0.01,2.84)	0.059

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race, occupation, ionizing radiation exposure, and lifetime cigarette smoking history because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the thyroid gland. Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

Table 10-22. Analysis of Malignant Systemic Neoplasms (Thyroid Gland) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	2 (0.2)		
Background RH	378	0 (0.0)	--	0.999[c]
Low RH	234	2 (0.9)	5.42 (0.76,38.74)	0.092
High RH	242	0 (0.0)	--	0.999[c]
Low plus High RH	476	2 (0.4)	--	0.680[c]

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a malignant systemic neoplasm of the thyroid gland.
--: Results not presented because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the thyroid gland.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,209		
Background RH	375	--	--
Low RH	232	5.18 (0.71,37.60)	0.104
High RH	240	--	--
Low plus High RH	472	--	--

[a] Relative risk and confidence interval relative to Comparisons.
--: Results not presented because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the thyroid gland.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for race, occupation, and ionizing radiation exposure because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the thyroid gland. Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

Table 10-22. Analysis of Malignant Systemic Neoplasms (Thyroid Gland) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	286	0 (0.0)	0.90 (0.34,2.40)	0.832
Medium	282	2 (0.7)		
High	286	0 (0.0)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
848	0.95 (0.34,2.70)	0.925

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race, occupation, ionizing radiation exposure, and lifetime cigarette smoking history because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the thyroid gland. Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

A significant inverse association between initial dioxin and a malignant systemic neoplasm of the thyroid gland was found from the Model 2 unadjusted analysis (Table 10-22(c): Est. RR=0.12, p=0.046). After adjustment for covariates, the result was marginally significant (Table 10-22(d): Adj. RR=0.12, p=0.059).

A marginally significant difference between Ranch Hands in the low dioxin category and Comparisons was observed in the unadjusted Model 3 analyses (Table 10-22(e): Est. RR=5.42, p=0.092). The occurrence of a malignant systemic neoplasm of the thyroid gland was higher for Ranch Hands in the low dioxin category than for Comparisons. The difference was nonsignificant after adjustment for covariates (Table 10-22(f): p=0.104). All other Model 3 contrasts, as well as the Model 4 analyses, were nonsignificant (Table 10-22(e,g-h): p≥0.68 for all remaining analyses).

10.2.2.1.23 Malignant Systemic Neoplasms (Bronchus and Lung)

Because of the sparse number of participants with a malignant systemic neoplasm of the bronchus or lung, analysis was limited. The unadjusted Model 1 analysis revealed a significant difference between Ranch Hands and Comparisons when examined across all occupations (Table 10-23(a): Est. RR=4.88, p=0.008). The results were marginally significant after adjustment for covariates (Table 10-23(b): Adj. RR=3.66, p=0.070). All other Model 1 contrasts were nonsignificant (Table 10-23(a,b): p>0.11).

Table 10-23. Analysis of Malignant Systemic Neoplasms (Bronchus and Lung)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***861***	***10 (1.2)***	***4.88 (1.34,17.79)***	***0.008***
	Comparison	***1,249***	***3 (0.2)***		
Officer	Ranch Hand	335	5 (1.5)	3.73 (0.72,19.33)	0.117
	Comparison	494	2 (0.4)		
Enlisted Flyer	Ranch Hand	149	3 (2.0)	3.82 (0.39,37.13)	0.248
	Comparison	187	1 (0.5)		
Enlisted Groundcrew	Ranch Hand	377	2 (0.5)	--	0.310[a]
	Comparison	568	0 (0.0)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a malignant systemic neoplasm of the bronchus and lung.
--: Results not presented because of the sparse number of participants with a malignant systemic neoplasm of the bronchus and lung.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***3.66 (0.78,17.13)***	***0.070***
Officer	3.51 (0.57,21.64)	0.176
Enlisted Flyer	2.58 (0.21,31.26)	0.456
Enlisted Groundcrew	--	--

--: Results not presented because of the sparse number of participants with a malignant systemic neoplasm of the bronchus and lung.

Note: Results are not adjusted for race because of the sparse number of participants with a malignant systemic neoplasm of the bronchus and lung.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	156	4 (2.6)	0.46 (0.20,1.04)	0.030
Medium	161	4 (2.5)		
High	159	0 (0.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

Table 10-23. Analysis of Malignant Systemic Neoplasms (Bronchus and Lung) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
n	Analysis Results for Log_2 (Initial Dioxin) Adjusted Relative Risk (95% C.I.)[a]	p-Value
472	0.53 (0.21,1.34)	0.144

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the bronchus and lung. Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	3 (0.3)		
Background RH	378	2 (0.5)	2.14 (0.35,12.94)	0.408
Low RH	234	8 (3.4)	14.26 (3.75,54.20)	<0.001
High RH	242	0 (0.0)	--	0.999[c]
Low plus High RH	476	8 (1.7)	--	0.003[c]

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a malignant systemic neoplasm of the bronchus and lung.
--: Results not presented because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the bronchus and lung.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 10-23. Analysis of Malignant Systemic Neoplasms (Bronchus and Lung) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,209		
Background RH	375	1.52 (0.21,11.09)	0.678
Low RH	232	8.67 (1.74,43.23)	0.008
High RH	240	--	--
Low plus High RH	472	--	--

[a] Relative risk and confidence interval relative to Comparisons.
--: Results not presented because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the bronchus and lung.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for race because of the sparse number of participants with a malignant systemic neoplasm of the bronchus and lung.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	286	1 (0.4)	0.98 (0.64,1.50)	0.915
Medium	282	6 (2.1)		
High	286	3 (1.1)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
847	1.15 (0.63,2.11)	0.638

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the bronchus and lung. Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

The Model 2 analysis of a malignant systemic neoplasm of the bronchus and lung revealed a significant inverse association with initial dioxin (Table 10-23(c): Est. RR=0.46, p=0.030). After adjustment for covariates, the association was nonsignificant (Table 10-23(d): p=0.144).

A significantly greater percentage of Ranch Hands in the low dioxin category had a malignant systemic neoplasm of the bronchus and lung than Comparisons in both the unadjusted and adjusted Model 3 analyses (Table 10-23(e): Est. RR=14.26, p<0.001; Adj. RR=8.67, p=0.008, respectively). The Model 4 unadjusted and adjusted analyses of malignant systemic neoplasms of the bronchus and lung revealed nonsignificant results (Table 10-23(g,h): p=0.638).

10.2.2.1.24 Malignant Systemic Neoplasms (Liver)

Because of the sparse number of participants with a malignant systemic neoplasm of the liver, analysis was limited. All Model 1 analyses were nonsignificant (Table 10-24(a,b): p>0.65). Results from the Model 2 analysis of malignant systemic neoplasms of the liver also were nonsignificant (Table 10-24(c,d): p≥0.14 for all analyses).

Table 10-24. Analysis of Malignant Systemic Neoplasms (Liver)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***861***	***2 (0.2)***	***1.45 (0.20,10.33)***	***0.710***
	Comparison	***1,249***	***2 (0.2)***		
Officer	Ranch Hand	335	0 (0.0)	--	0.999[a]
	Comparison	494	1 (0.2)		
Enlisted Flyer	Ranch Hand	149	1 (0.7)	--	0.909[a]
	Comparison	187	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	377	1 (0.3)	1.51 (0.09,24.18)	0.772
	Comparison	568	1 (0.2)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a malignant systemic neoplasm of the liver.
--: Results not presented because of the sparse number of participants with a malignant systemic neoplasm of the liver.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.57 (0.22,11.35)***	***0.655***
Officer	--	--
Enlisted Flyer	--	--
Enlisted Groundcrew	1.72 (0.11,27.93)	0.703

--: Results not presented because of the sparse number of participants with a malignant systemic neoplasm of the liver.

Note: Results are not adjusted for race because of the sparse number of participants with a malignant systemic neoplasm of the liver. Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

Table 10-24. Analysis of Malignant Systemic Neoplasms (Liver) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	156	0 (0.0)	1.76 (0.73,4.22)	0.231
Medium	161	1 (0.6)		
High	159	1 (0.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
472	2.06 (0.82,5.15)	0.140

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race, occupation, and ionizing radiation exposure because of the sparse number of participants with a malignant systemic neoplasm of the liver. Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	2 (0.2)		
Background RH	378	0 (0.0)	--	0.999[c]
Low RH	234	0 (0.0)	--	0.999[c]
High RH	242	2 (0.8)	5.70 (0.78,41.53)	0.086
Low plus High RH	476	2 (0.4)	--	0.680[c]

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a malignant systemic neoplasm of the liver.
--: Results not presented because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the liver.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 10-24. Analysis of Malignant Systemic Neoplasms (Liver) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,209		
Background RH	375	--	--
Low RH	232	--	--
High RH	240	7.06 (0.70,71.25)	0.098
Low plus High RH	472	--	--

[a] Relative risk and confidence interval relative to Comparisons.
--: Results not presented because of the sparse number of participants with a malignant systemic neoplasm of the liver.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for race because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the liver. Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	286	0 (0.0)	2.10 (0.92,4.78)	0.080
Medium	282	0 (0.0)		
High	286	2 (0.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
847	2.52 (1.03,6.15)	0.042

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race, occupation, and ionizing radiation exposure because of the sparse number of participants with a malignant systemic neoplasm of the liver. Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

The unadjusted and adjusted Model 3 analyses displayed a marginally significant difference between Ranch Hands in the high dioxin category and Comparisons (Table 10-24(e,f): Est. RR=5.70, p=0.086; Adj. RR=7.06, p=0.098, respectively). The percentage of Ranch Hands in the high dioxin category with a malignant systemic neoplasm of the liver was greater than the percentage of Comparisons. The results in all other Model 3 unadjusted analyses were nonsignificant (Table 10-24(e): p≥0.68).

The Model 4 unadjusted analysis revealed a marginally significant positive association between 1987 dioxin levels and a malignant systemic neoplasm of the liver (Table 10-24(g): Est. RR=2.10, p=0.080). After adjustment for covariates, the result was significant (Table 10-24(h): Est. RR=2.52, p=0.042).

10.2.2.1.25 Malignant Systemic Neoplasms (Colon and Rectum)

All results from the analyses of malignant systemic neoplasms of the colon and rectum from Models 1, 2, and 4 were nonsignificant (Table 10-25(a-d,g-h): p>0.29 for each analysis).

Table 10-25. Analysis of Malignant Systemic Neoplasms (Colon and Rectum)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***861***	***7 (0.8)***	***1.27 (0.46,3.52)***	***0.645***
	Comparison	***1,249***	***8 (0.6)***		
Officer	Ranch Hand	335	3 (0.9)	2.22 (0.37,13.38)	0.383
	Comparison	494	2 (0.4)		
Enlisted Flyer	Ranch Hand	149	2 (1.3)	1.26 (0.18,9.04)	0.819
	Comparison	187	2 (1.1)		
Enlisted Groundcrew	Ranch Hand	377	2 (0.5)	0.75 (0.14,4.13)	0.743
	Comparison	568	4 (0.7)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.50 (0.41,5.47)***	***0.536***
Officer	2.59 (0.37,17.95)	0.335
Enlisted Flyer	1.57 (0.19,13.30)	0.678
Enlisted Groundcrew	0.85 (0.13,5.78)	0.872

Note: Results are not adjusted for race because of the sparse number of participants with a malignant systemic neoplasm of the colon and rectum.

Table 10-25. Analysis of Malignant Systemic Neoplasms (Colon and Rectum) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	156	0 (0.0)	0.76 (0.39,1.49)	0.405
Medium	161	5 (3.1)		
High	159	1 (0.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
472	0.93 (0.42,2.07)	0.855

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the colon and rectum. Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	8 (0.7)		
Background RH	378	1 (0.3)	0.49 (0.06,3.94)	0.500
Low RH	234	5 (2.1)	3.02 (0.97,9.45)	0.057
High RH	242	1 (0.4)	0.51 (0.06,4.15)	0.528
Low plus High RH	476	6 (1.3)	1.22 (0.33,4.51)	0.764

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 10-25. Analysis of Malignant Systemic Neoplasms (Colon and Rectum) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,209		
Background RH	375	0.60 (0.06,5.76)	0.658
Low RH	232	3.28 (0.77,13.90)	0.107
High RH	240	0.57 (0.05,5.85)	0.632
Low plus High RH	472	1.34 (0.27,6.56)	0.717

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for race because of the sparse number of participants with a malignant systemic neoplasm of the colon and rectum.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	286	1 (0.4)	1.18 (0.74,1.91)	0.495
Medium	282	2 (0.7)		
High	286	4 (1.4)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
847	1.44 (0.72,2.86)	0.291

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the colon and rectum. Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

The Model 3 unadjusted analysis of malignant systemic neoplasms of the colon and rectum displayed a marginally significant difference between Ranch Hands in the low dioxin category and Comparisons. The occurrence of a malignant systemic neoplasm of the colon and rectum was higher for Ranch Hands in the low dioxin category than for Comparisons (Table 10-25(e): Est. RR=3.02, p=0.057). The result was

nonsignificant after adjustment for covariates (Table 10-25(f): p=0.107). All other Model 3 contrasts were nonsignificant (Table 10-25(e,f): p≥0.50).

10.2.2.1.26 Malignant Systemic Neoplasms (Kidney and Bladder)

Because of the sparse number of participants with a history of a malignant systemic neoplasm of the kidney or bladder, analysis was limited. Across all occupations, the difference between Ranch Hands and Comparisons was significant, with more malignant systemic neoplasms of the kidney and bladder occurring in Ranch Hands than in Comparisons (Table 10-26(a): Est. RR=2.68, p=0.046). After adjustment for covariates, the result was marginally significant (Table 10-26(b): Adj. RR=3.12, p=0.061). All other Model 1 contrasts, as well as the results from the Model 2 and Model 4 analyses, were nonsignificant (Table 10-26(a-d,g-h): p>0.17).

Table 10-26. Analysis of Malignant Systemic Neoplasms (Kidney and Bladder)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***861***	***11 (1.3)***	***2.68 (0.99,7.28)***	***0.046***
	Comparison	***1,249***	***6 (0.5)***		
Officer	Ranch Hand	335	5 (1.5)	1.48 (0.43,5.16)	0.537
	Comparison	494	5 (1.0)		
Enlisted Flyer	Ranch Hand	149	3 (2.0)	--	0.172[a]
	Comparison	187	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	377	3 (0.8)	4.55 (0.47,43.89)	0.190
	Comparison	568	1 (0.2)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a malignant systemic neoplasm of the kidney and bladder.
--: Results not presented because of the sparse number of participants with a malignant systemic neoplasm of the kidney and bladder.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***3.12 (0.88,11.04)***	***0.061***
Officer	1.86 (0.43,8.16)	0.409
Enlisted Flyer	--	--
Enlisted Groundcrew	4.20 (0.36,49.46)	0.254

--: Results not presented because of the sparse number of participants with a malignant systemic neoplasm of the kidney and bladder.

Table 10-26. Analysis of Malignant Systemic Neoplasms (Kidney and Bladder) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	156	2 (1.3)	0.72 (0.37,1.41)	0.312
Medium	161	4 (2.5)		
High	159	1 (0.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
472	1.05 (0.47,2.38)	0.899

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	6 (0.5)		
Background RH	378	4 (1.1)	2.04 (0.57,7.34)	0.273
Low RH	234	5 (2.1)	4.44 (1.34,14.69)	0.015
High RH	242	2 (0.8)	1.75 (0.35,8.75)	0.497
Low plus High RH	476	7 (1.5)	2.76 (0.87,8.80)	0.085

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 10-26. Analysis of Malignant Systemic Neoplasms (Kidney and Bladder) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,209		
Background RH	375	2.26 (0.49,10.35)	0.292
Low RH	232	4.44 (1.04,18.95)	0.044
High RH	240	3.26 (0.46,23.17)	0.237
Low plus High RH	472	3.80 (0.88,16.46)	0.075

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	286	3 (1.1)	1.03 (0.69,1.53)	0.902
Medium	282	5 (1.8)		
High	286	3 (1.1)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
847	1.14 (0.66,1.96)	0.634

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

A significantly greater percentage of Ranch Hands in the low dioxin category had a malignant systemic neoplasm of the kidney and bladder than Comparisons in both the unadjusted and adjusted Model 3 analyses (Table 10-26(e,f): Est. RR=4.44, p=0.015; Adj. RR=4.44, p=0.044, respectively). The results were marginally significant when Ranch Hands in the low and high dioxin categories were combined (Table 10-26(e,f): Est. RR=2.76, p=0.085; Adj. RR=3.80, p=0.075, respectively). All other Model 3 contrasts were nonsignificant (Table 10-26(e,f): p>0.23).

10.2.2.1.27 Malignant Systemic Neoplasms (Prostate)

All results from the Model 1 analysis of malignant systemic neoplasms of the prostate were nonsignificant (Table 10-27(a,b): p>0.15).

A significant inverse association between initial dioxin and malignant systemic neoplasms of the prostate was found in the unadjusted Model 2 analysis (Table 10-27(c): Est. RR=0.52, p=0.007). After adjustment for covariates, the association was nonsignificant (Table 10-27(d): p=0.254).

Table 10-27. Analysis of Malignant Systemic Neoplasms (Prostate)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***861***	***26 (3.0)***	***0.97 (0.58,1.60)***	***0.893***
	Comparison	***1,249***	***39 (3.1)***		
Officer	Ranch Hand	335	13 (3.9)	0.76 (0.38,1.50)	0.427
	Comparison	494	25 (5.1)		
Enlisted Flyer	Ranch Hand	149	7 (4.7)	2.26 (0.65,7.86)	0.201
	Comparison	187	4 (2.1)		
Enlisted Groundcrew	Ranch Hand	377	6 (1.6)	0.90 (0.33,2.50)	0.844
	Comparison	568	10 (1.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.69 (0.38,1.25)***	***0.219***
Officer	0.58 (0.27,1.22)	0.151
Enlisted Flyer	1.54 (0.41,5.75)	0.521
Enlisted Groundcrew	0.59 (0.19,1.84)	0.360

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	156	8 (5.1)	0.52 (0.30,0.89)	0.007
Medium	161	7 (4.4)		
High	159	1 (0.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

Table 10-27. Analysis of Malignant Systemic Neoplasms (Prostate) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
n	Analysis Results for Log_2 (Initial Dioxin) Adjusted Relative Risk (95% C.I.)[a]	p-Value
472	0.68 (0.33,1.37)	0.254

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the prostate. Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	39 (3.2)		
Background RH	378	9 (2.4)	0.73 (0.35,1.52)	0.398
Low RH	234	12 (5.1)	1.63 (0.84,3.16)	0.150
High RH	242	4 (1.7)	0.51 (0.18,1.44)	0.202
Low plus High RH	476	16 (3.4)	0.90 (0.46,1.75)	0.757

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,209		
Background RH	375	0.48 (0.21,1.07)	0.072
Low RH	232	0.91 (0.42,1.97)	0.818
High RH	240	0.61 (0.19,1.93)	0.404
Low plus High RH	472	0.75 (0.35,1.60)	0.453

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 10-27. Analysis of Malignant Systemic Neoplasms (Prostate) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	286	7 (2.5)	0.82 (0.62,1.10)	0.182
Medium	282	12 (4.3)		
High	286	6 (2.1)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
847	0.83 (0.56,1.23)	0.353

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

The Model 3 adjusted analysis revealed a marginally significant difference in malignant systemic neoplasms of the prostate between Ranch Hands in the background dioxin category and Comparisons (Table 10-27(f): Adj. RR=0.48, p=0.072). More Comparisons than Ranch Hands had a malignant systemic neoplasm of the prostate. All other Model 3 contrasts and the results from the Model 4 analyses were nonsignificant (Table 10-27(e-h): p≥0.15 for all remaining analyses).

10.2.2.1.28 Malignant Systemic Neoplasms (Testicles)

Because of the sparse number of participants with a malignant systemic neoplasm of the testicles, analysis was limited. All Model 1 analyses were nonsignificant (Table 10-28(a): p>0.13 for each contrast examined). Results from Model 2 analyses also were nonsignificant (Table 10-28(c,d): p>0.41).

Table 10-28. Analysis of Malignant Systemic Neoplasms (Testicles)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***861***	***3 (0.4)***	--	***0.134***[a]
	Comparison	***1,249***	***0 (0.0)***		
Officer	Ranch Hand	335	1 (0.3)	--	0.845[a]
	Comparison	494	0 (0.0)		
Enlisted Flyer	Ranch Hand	149	1 (0.7)	--	0.909[a]
	Comparison	187	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	377	1 (0.3)	--	0.836[a]
	Comparison	568	0 (0.0)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a malignant systemic neoplasm of the testicles.
--: Results not presented because of the sparse number of participants with a malignant systemic neoplasm of the testicles.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	--	--
Officer	--	--
Enlisted Flyer	--	--
Enlisted Groundcrew	--	--

--: Results not presented because of the sparse number of participants with a malignant systemic neoplasm of the testicles.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	156	1 (0.6)	0.65 (0.21,1.98)	0.413
Medium	161	2 (1.2)		
High	159	0 (0.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

Table 10-28. Analysis of Malignant Systemic Neoplasms (Testicles) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
n	Analysis Results for Log_2 (Initial Dioxin) Adjusted Relative Risk (95% C.I.)[a]	p-Value
472	0.77 (0.22,2.64)	0.663

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race and ionizing radiation exposure because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the testicles. Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
Comparison	1,211	0 (0.0)		
Background RH	378	0 (0.0)	--	--
Low RH	234	2 (0.9)	--	0.024[a]
High RH	242	1 (0.4)	--	0.371[a]
Low plus High RH	476	3 (0.6)	--	0.034[a]

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a malignant systemic neoplasm of the testicles.
--: Results not presented because of the sparse number of participants with a malignant systemic neoplasm of the testicles.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
Comparison	--		
Background RH	--	--	--
Low RH	--	--	--
High RH	--	--	--
Low plus High RH	--	--	--

--: Results not presented because of the sparse number of participants with a malignant systemic neoplasm of the testicles.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 10-28. Analysis of Malignant Systemic Neoplasms (Testicles) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	286	0 (0.0)	1.22 (0.59,2.50)	0.599
Medium	282	1 (0.4)		
High	286	2 (0.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
847	1.35 (0.54,3.37)	0.517

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race and ionizing radiation exposure because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the testicles. Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

Significant differences were found in the unadjusted Model 3 analysis between Ranch Hands in the low dioxin category and Comparisons, and between Ranch Hands in the low plus high dioxin category and Comparisons (Table 10-28(e,f): p=0.024 and p=0.034, respectively). More Ranch Hands had a malignant systemic neoplasm of the testicles than did Comparisons. The adjusted Model 3 analysis was not possible because of the sparse number of neoplasms of the testicles. The remaining unadjusted Model 3 contrast and the Model 4 analyses were nonsignificant (Table 10-28(e,g-h): p>0.37 for each remaining analysis).

10.2.2.1.29 Malignant Systemic Neoplasms (Extrahepatic Bile Duct)

Because of the presence of a malignant systemic neoplasm of the extrahepatic bile duct in only one Ranch Hand, statistical analysis was not possible. This participant was a non-Black enlisted flyer.

10.2.2.1.30 Malignant Systemic Neoplasms (Ill-Defined Sites)

Only one Comparison had a malignant systemic neoplasm of ill-defined sites, which precluded statistical analysis. This Comparison was a non-Black enlisted flyer.

10.2.2.1.31 Malignant Systemic Neoplasms (Connective and Other Soft Tissues)

Because of the sparse number of participants with a malignant systemic neoplasm of the connective or other soft tissues, analysis was limited. All results from the analyses performed were nonsignificant (Table 10-29(a-h): p>0.15 for each analysis).

Table 10-29. Analysis of Malignant Systemic Neoplasms (Connective and Other Soft Tissues)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***861***	***1 (0.1)***	***0.73 (0.07,8.01)***	***0.790***
	Comparison	***1,249***	***2 (0.2)***		
Officer	Ranch Hand	335	0 (0.0)	--	--
	Comparison	494	0 (0.0)		
Enlisted Flyer	Ranch Hand	149	1 (0.7)	--	0.909[a]
	Comparison	187	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	377	0 (0.0)	--	0.667[a]
	Comparison	568	2 (0.4)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a malignant systemic neoplasm of connective and other soft tissues.
--: Results not presented because of the sparse number of participants with a malignant systemic neoplasm of connective and other soft tissues.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.79 (0.05,12.82)***	***0.870***
Officer	--	--
Enlisted Flyer	--	--
Enlisted Groundcrew	--	--

--: Results not presented because of the sparse number of participants with a malignant systemic neoplasm of connective and other soft tissues.

Note: Results are not adjusted for race because of the sparse number of participants with a malignant systemic neoplasm of connective and other soft tissues.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	156	0 (0.0)	2.44 (0.70,8.47)	0.168
Medium	161	0 (0.0)		
High	159	1 (0.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

Table 10-29. Analysis of Malignant Systemic Neoplasms (Connective and Other Soft Tissues) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
475	2.39 (0.68,8.37)	0.179

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for age, race, occupation, ionizing radiation exposure, and lifetime alcohol history because of the sparse number of Ranch Hands with a malignant systemic neoplasm of connective and other soft tissues. Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	**n**	**Number (%) Yes**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,211	2 (0.2)		
Background RH	378	0 (0.0)	--	0.999[c]
Low RH	234	0 (0.0)	--	0.999[c]
High RH	242	1 (0.4)	2.34 (0.21,26.43)	0.493
Low plus High RH	476	1 (0.2)	--	0.999[c]

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a malignant systemic neoplasm of connective and other soft tissues.
--: Results not presented because of the sparse number of Ranch Hands with a malignant systemic neoplasm of connective and other soft tissues.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 10-29. Analysis of Malignant Systemic Neoplasms (Connective and Other Soft Tissues) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,209		
Background RH	375	--	--
Low RH	232	--	--
High RH	240	3.17 (0.17,57.71)	0.436
Low plus High RH	472	--	--

[a] Relative risk and confidence interval relative to Comparisons.
--: Results not presented because of the sparse number of Ranch Hands with a malignant systemic neoplasm of connective and other soft tissues.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	286	0 (0.0)	2.36 (0.73,7.65)	0.151
Medium	282	0 (0.0)		
High	286	1 (0.4)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
852	2.36 (0.72,7.79)	0.155

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for age, race, occupation, ionizing radiation exposure, and lifetime alcohol history because of the sparse number of Ranch Hands with a malignant systemic neoplasm of connective and other soft tissues. Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

10.2.2.1.32 Carcinoma In Situ (Penis)

Because of the presence of carcinoma in situ of the penis in only one Comparison and no Ranch Hands, statistical analysis was not performed. The Comparison was a non-Black enlisted groundcrew.

10.2.2.1.33 Hodgkin's Disease

Because of the sparse number of participants with a history of Hodgkin's disease, analysis was limited. All results were nonsignificant (Table 10-30(a-h): p>0.29 for each analysis).

Table 10-30. Analysis of Hodgkin's Disease

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***861***	***1 (0.1)***	***0.48 (0.05,4.65)***	***0.507***
	Comparison	***1,249***	***3 (0.2)***		
Officer	Ranch Hand	335	1 (0.3)	0.74 (0.07,8.16)	0.803
	Comparison	494	2 (0.4)		
Enlisted Flyer	Ranch Hand	149	0 (0.0)	--	--
	Comparison	187	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	377	0 (0.0)	--	0.999[a]
	Comparison	568	1 (0.2)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of Ranch Hands with Hodgkin's disease.
--: Results not presented because of the sparse number of Ranch Hands with Hodgkin's disease.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.29 (0.03,3.23)***	***0.291***
Officer	0.47 (0.04,5.86)	0.554
Enlisted Flyer	--	--
Enlisted Groundcrew	--	--

--: Results not presented because of the sparse number of Ranch Hands with Hodgkin's disease.

Note: Results are not adjusted for race because of the sparse number of participants with Hodgkin's disease. Results for all occupations combined also are not adjusted for occupation because of the sparse number of participants with Hodgkin's disease.

Table 10-30. Analysis of Hodgkin's Disease (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)	p-Value
Low	156	0 (0.0)	--	--
Medium	161	0 (0.0)		
High	159	0 (0.0)		

--: Results not presented because of the sparse number of Ranch Hands with Hodgkin's disease.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)	p-Value
--	--	--

--: Results not presented because of the sparse number of Ranch Hands with Hodgkin's disease.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	3 (0.3)		
Background RH	378	1 (0.3)	0.92 (0.09,9.02)	0.945
Low RH	234	0 (0.0)	--	0.999[c]
High RH	242	0 (0.0)	--	0.999[c]
Low plus High RH	476	0 (0.0)	--	0.656[c]

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] P-value determined using a chi-square test with continuity correction because of the sparse number of Ranch Hands with Hodgkin's disease.
--: Results not presented because of the sparse number of Ranch Hands with Hodgkin's disease.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 10-30. Analysis of Hodgkin's Disease (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,209		
Background RH	375	0.55 (0.05,6.15)	0.624
Low RH	232	--	--
High RH	240	--	--
Low plus High RH	472	--	--

[a] Relative risk and confidence interval relative to Comparisons.
--: Results not presented because of the sparse number of Ranch Hands with Hodgkin's disease.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for occupation and race because of the sparse number of participants with Hodgkin's disease.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	286	1 (0.4)	0.67 (0.15,2.97)	0.583
Medium	282	0 (0.0)		
High	286	0 (0.0)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
848	0.70 (0.08,6.51)	0.745

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race, occupation, and ionizing radiation exposure because of the sparse number of Ranch Hands with Hodgkin's disease. Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

10.2.2.1.34 Non-Hodgkin's Lymphoma

Because of the sparse number of participants with non-Hodgkin's lymphoma, analysis was limited. All results were nonsignificant (Table 10-31(a-h): p>0.18 for each analysis).

Table 10-31. Analysis of Non-Hodgkin's Lymphoma

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***861***	***1 (0.1)***	***0.48 (0.05,4.65)***	***0.507***
	Comparison	***1,249***	***3 (0.2)***		
Officer	Ranch Hand	335	0 (0.0)	--	0.657[a]
	Comparison	494	2 (0.4)		
Enlisted Flyer	Ranch Hand	149	0 (0.0)	--	--
	Comparison	187	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	377	1 (0.3)	1.51 (0.09,24.18)	0.772
	Comparison	568	1 (0.2)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of Ranch Hands with non-Hodgkin's lymphoma.
--: Results not presented because of the sparse number of Ranch Hands with non-Hodgkin's lymphoma.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.18 (0.01,2.61)***	***0.186***
Officer	--	--
Enlisted Flyer	--	--
Enlisted Groundcrew	0.61 (0.02,15.18)	0.762

--: Results not presented because of the sparse number of Ranch Hands with non-Hodgkin's lymphoma.

Note: Results are not adjusted for race because of the sparse number of participants with non-Hodgkin's lymphoma. Results for all occupations combined also are not adjusted for occupation because of the sparse number of participants with non-Hodgkin's lymphoma.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)	p-Value
Low	156	0 (0.0)	--	--
Medium	161	0 (0.0)		
High	159	0 (0.0)		

--: Results not presented because of the sparse number of Ranch Hands with non-Hodgkin's lymphoma.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

Table 10-31. Analysis of Non-Hodgkin's Lymphoma (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)	p-Value
--	--	--

--: Results not presented because of the sparse number of Ranch Hands with non-Hodgkin's lymphoma.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	3 (0.3)		
Background RH	378	1 (0.3)	0.92 (0.09,9.02)	0.944
Low RH	234	0 (0.0)	--	0.999[c]
High RH	242	0 (0.0)	--	0.999[c]
Low plus High RH	476	0 (0.0)	--	0.656[c]

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] P-value determined using a chi-square test with continuity correction because of the sparse number of Ranch Hands with non-Hodgkin's lymphoma.
--: Results not presented because of the sparse number of Ranch Hands with non-Hodgkin's lymphoma.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,209		
Background RH	375	0.24 (0.01,4.90)	0.351
Low RH	232	--	--
High RH	240	--	--
Low plus High RH	472	--	--

[a] Relative risk and confidence interval relative to Comparisons.
--: Results not presented because of the sparse number of Ranch Hands with non-Hodgkin's lymphoma.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for race and occupation because of the sparse number of Ranch Hands with non-Hodgkin's lymphoma.

Table 10-31. Analysis of Non-Hodgkin's Lymphoma (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	286	1 (0.4)	0.60 (0.13,2.70)	0.491
Medium	282	0 (0.0)		
High	286	0 (0.0)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
852	0.31 (0.01,7.88)	0.443

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race, occupation, ionizing radiation exposure, and lifetime alcohol history because of the sparse number of Ranch Hands with non-Hodgkin's lymphoma. Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

10.2.2.1.35 Other Malignant Systemic Neoplasms of Lymphoid and Histiocytic Tissue

Because of the sparse number of participants with other malignant systemic neoplasms of lymphoid and histiocytic tissue, analysis was limited. All results were nonsignificant (Table 10-32 (a-h): p>0.33 for each analysis).

Table 10-32. Analysis of Other Malignant Systemic Neoplasms of Lymphoid and Histiocytic Tissue

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***861***	***2 (0.2)***	***0.72 (0.13,3.97)***	***0.706***
	Comparison	***1,249***	***4 (0.3)***		
Officer	Ranch Hand	335	1 (0.3)	0.74 (0.07,8.16)	0.803
	Comparison	494	2 (0.4)		
Enlisted Flyer	Ranch Hand	149	0 (0.0)	--	0.999[a]
	Comparison	187	1 (0.5)		
Enlisted Groundcrew	Ranch Hand	377	1 (0.3)	1.51 (0.09,24.18)	0.772
	Comparison	568	1 (0.2)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of Ranch Hands with a malignant systemic neoplasm of lymphoid and histiocytic tissue.
--: Results not presented because of the sparse number of Ranch Hands with a malignant systemic neoplasm of lymphoid and histiocytic tissue.

Table 10-32. Analysis of Other Malignant Systemic Neoplasms of Lymphoid and Histiocytic Tissue (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.70 (0.10,5.03)***	***0.724***
Officer	0.69 (0.05,9.34)	0.781
Enlisted Flyer	--	--
Enlisted Groundcrew	1.57 (0.08,31.01)	0.767

--: Results not presented because of the sparse number of Ranch Hands with a malignant systemic neoplasm of lymphoid and histiocytic tissue.

Note: Results are not adjusted for race because of the sparse number of participants with a malignant systemic neoplasm of lymphoid and histiocytic tissue.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)	p-Value
Low	160	0 (0.0)	--	--
Medium	162	0 (0.0)		
High	160	0 (0.0)		

--: Results not presented because of the sparse number of Ranch Hands with a malignant systemic neoplasm of lymphoid and histiocytic tissue.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)	p-Value
--	--	--

--: Results not presented because of the sparse number of Ranch Hands with a malignant systemic neoplasm of lymphoid and histiocytic tissue.

Table 10-32. Analysis of Other Malignant Systemic Neoplasms of Lymphoid and Histiocytic Tissue (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	**n**	**Number (%) Yes**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,211	2 (0.2)		
Background RH	378	2 (0.5)	2.64 (0.37,19.03)	0.336
Low RH	234	0 (0.0)	--	0.999[c]
High RH	242	0 (0.0)	--	0.999[c]
Low plus High RH	476	0 (0.0)	--	0.919[c]

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] P-value determined using a chi-square test with continuity correction because of the sparse number of Ranch Hands with a malignant systemic neoplasm of lymphoid and histiocytic tissue.
--: Results not presented because of the sparse number of Ranch Hands with a malignant systemic neoplasm of lymphoid and histiocytic tissue.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Comparison	1,209		
Background RH	375	1.90 (0.15,23.45)	0.618
Low RH	232	--	--
High RH	240	--	--
Low plus High RH	472	--	--

[a] Relative risk and confidence interval relative to Comparisons.
--: Results not presented because of the sparse number of Ranch Hands with a malignant systemic neoplasm of lymphoid and histiocytic tissue.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for race because of the sparse number of participants with a malignant systemic neoplasm of lymphoid and histiocytic tissue.

Table 10-32. Analysis of Other Malignant Systemic Neoplasms of Lymphoid and Histiocytic Tissue (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	286	1 (0.4)	0.68 (0.24,1.96)	0.466
Medium	282	1 (0.4)		
High	286	0 (0.0)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
847	0.63 (0.09,4.17)	0.580

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race, occupation, and ionizing radiation exposure because of the sparse number of Ranch Hands with a malignant systemic neoplasm of lymphoid and histiocytic tissue. Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

10.2.2.1.36 All Malignant Skin and Systemic Neoplasms

A marginally significant difference between Ranch Hands and Comparisons was found in the unadjusted Model 1 analysis of all skin and systemic neoplasms for all occupations combined (Table 10-33(a): Est. RR=1.20, p=0.099). The contrast of Ranch Hand and Comparisons enlisted flyers was significant in the unadjusted Model 1 analysis (Table 10-33(a): Est. RR=1.78, p=0.034). More Ranch Hands than Comparisons exhibited a history of a malignant skin or systemic neoplasm. After adjustment for covariates, both results were nonsignificant (Table 10-33(b): p>0.10 for each contrast). All other Model 1 contrasts were nonsignificant (Table 10-33(a,b): p>0.11).

Table 10-33. Analysis of All Malignant Skin and Systemic Neoplasms

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***851***	***186 (21.9)***	***1.20 (0.97,1.49)***	***0.099***
	Comparison	***1,238***	***234 (18.9)***		
Officer	Ranch Hand	330	95 (28.8)	1.29 (0.94,1.77)	0.112
	Comparison	487	116 (23.8)		
Enlisted Flyer	Ranch Hand	148	39 (26.4)	1.78 (1.04,3.02)	0.034
	Comparison	185	31 (16.8)		
Enlisted Groundcrew	Ranch Hand	373	52 (13.9)	0.89 (0.62,1.29)	0.546
	Comparison	566	87 (15.4)		

Table 10-33. Analysis of All Malignant Skin and Systemic Neoplasms (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1.06 (0.80,1.41)*	*0.668*
Officer	1.14 (0.79,1.65)	0.470
Enlisted Flyer	1.63 (0.91,2.92)	0.103
Enlisted Groundcrew	0.78 (0.51,1.19)	0.247

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	150	41 (27.3)	0.74 (0.62,0.89)	0.001
Medium	160	45 (28.1)		
High	159	23 (14.5)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
n	Analysis Results for Log_2 (Initial Dioxin) Adjusted Relative Risk (95% C.I.)[a]	p-Value
465	0.91 (0.72,1.14)	0.396

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,200	226 (18.8)		
Background RH	375	76 (20.3)	1.12 (0.83,1.49)	0.464
Low RH	228	68 (29.8)	1.82 (1.33,2.51)	<0.001
High RH	241	41 (17.0)	0.87 (0.60,1.26)	0.457
Low plus High RH	469	109 (23.2)	1.25 (0.96,1.62)	0.103

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 10-33. Analysis of All Malignant Skin and Systemic Neoplasms (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,196		
Background RH	372	0.84 (0.60,1.20)	0.339
Low RH	226	1.51 (1.03,2.21)	0.035
High RH	239	1.01 (0.66,1.57)	0.952
Low plus High RH	465	1.23 (0.88,1.71)	0.221

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	284	57 (20.1)	0.94 (0.84,1.05)	0.281
Medium	275	74 (26.9)		
High	285	54 (19.0)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
837	1.10 (0.94,1.27)	0.227

[a] Relative risk for a twofold increase in 1987 dioxin.

The unadjusted analysis of Model 2 displayed a significant inverse relation between initial dioxin and malignant skin and systemic neoplasms (Table 10-33(c): Est. RR=0.74, p=0.001). After adjustment for covariates, the association was nonsignificant (Table 10-33(d): p=0.396).

Both the unadjusted and adjusted Model 3 analyses revealed a significant difference in malignant skin and systemic neoplasms between Ranch Hands in the low dioxin category and Comparisons (Table 10-33(e,f): Est. RR=1.82, p<0.001; Adj. RR=1.51, p=0.035, respectively). More Ranch Hands in the low dioxin category than Comparisons had a malignant skin and systemic neoplasm. All other Model 3 contrasts and all results from the Model 4 analysis were nonsignificant (Table 10-33(e-h): p>0.10 for each analysis).

10.2.2.1.37 All Skin and Systemic Neoplasms

The Model 1 unadjusted analysis of all skin and systemic neoplasms revealed a significant difference between Ranch Hands and Comparisons when examined across all occupations (Table 10-34(a): Est. RR=1.25, p=0.014). A marginally significant difference within officers also was found in the unadjusted analysis (Table 10-34(a): Est. RR=1.29, p=0.079). Both contrasts showed more Ranch Hands than Comparisons with a history of a skin or systemic neoplasm. The contrasts were nonsignificant after adjustment for covariates (Table 10-34(b): p>0.72 for each contrast). All other Model 1 contrasts were also nonsignificant (Table 10-34(a,b): p>0.15).

A significant inverse association between initial dioxin and the occurrence of a skin or systemic neoplasm was found in the Model 2 unadjusted analysis (Table 10-34(c): Est. RR=0.84, p=0.017). After adjustment for covariates, the result was nonsignificant (Table 10-34(d): p=0.244).

Table 10-34. Analysis of All Skin and Systemic Neoplasms

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***847***	***473 (55.8)***	***1.25 (1.05,1.49)***	***0.014***
	Comparison	***1,231***	***620 (50.4)***		
Officer	Ranch Hand	329	202 (61.4)	1.29 (0.97,1.72)	0.079
	Comparison	482	266 (55.2)		
Enlisted Flyer	Ranch Hand	146	84 (57.5)	1.37 (0.88,2.12)	0.158
	Comparison	185	92 (49.7)		
Enlisted Groundcrew	Ranch Hand	372	187 (50.3)	1.17 (0.90,1.51)	0.253
	Comparison	564	262 (46.5)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.04 (0.83,1.30)***	***0.756***
Officer	1.06 (0.77,1.46)	0.725
Enlisted Flyer	1.15 (0.72,1.84)	0.557
Enlisted Groundcrew	0.98 (0.72,1.33)	0.881

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	150	92 (61.3)	0.84 (0.73,0.97)	0.017
Medium	159	95 (59.8)		
High	157	72 (45.9)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

Table 10-34. Analysis of All Skin and Systemic Neoplasms (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
n	Analysis Results for Log_2 (Initial Dioxin) Adjusted Relative Risk (95% C.I.)[a]	p-Value
463	0.90 (0.76,1.07)	0.244

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,193	602 (50.5)		
Background RH	374	211 (56.4)	1.30 (1.03,1.64)	0.030
Low RH	227	137 (60.4)	1.49 (1.11,1.99)	0.007
High RH	239	122 (51.1)	1.01 (0.76,1.33)	0.969
Low plus High RH	466	259 (55.6)	1.22 (0.98,1.51)	0.076

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,189		
Background RH	371	1.01 (0.76,1.33)	0.956
Low RH	225	1.15 (0.83,1.61)	0.396
High RH	238	0.93 (0.67,1.30)	0.684
Low plus High RH	463	1.04 (0.79,1.35)	0.799

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 10-34. Analysis of All Skin and Systemic Neoplasms (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	283	161 (56.9)	0.93 (0.85,1.02)	0.149
Medium	275	163 (59.3)		
High	282	146 (51.8)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
834	0.99 (0.88,1.11)	0.854

[a] Relative risk for a twofold increase in 1987 dioxin.

In the Model 3 unadjusted analysis, a significantly higher percentage of Ranch Hands in the background, low, and low plus high dioxin categories had an occurrence of a skin or systemic neoplasm, relative to Comparisons (Table 10-34(e): Est. RR=1.30; p=0.030; Est. RR=1.49, p=0.007; and Est. RR=1.22, p=0.076, respectively). After adjustment for covariates, results were nonsignificant for each contrast (Table 10-34(f): p>0.39 for each adjusted contrast). All other Model 3 contrasts and the results from the Model 4 analysis were nonsignificant (Table 10-34(e-h): p>0.14 for each remaining analysis).

10.2.2.2 Laboratory Examination Variables

10.2.2.2.1 Prostate-Specific Antigen (PSA) (Continuous)

All results from the Model 1 unadjusted and adjusted analyses of continuous PSA were nonsignificant (Table 10-35(a,b): p≥0.59 for all Model 1 analyses).

Table 10-35. Analysis of PSA (ng/ml) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***829***	***1.104***	–0.016 --	***0.671***
	Comparison	***1,190***	***1.120***		
Officer	Ranch Hand	320	1.195	–0.034 --	0.613
	Comparison	458	1.229		
Enlisted Flyer	Ranch Hand	141	1.241	0.007 --	0.949
	Comparison	180	1.234		
Enlisted Groundcrew	Ranch Hand	368	0.985	–0.020 --	0.693
	Comparison	552	1.005		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***823***	***1.202***	***0.003 --***	***0.946***
	Comparison	***1,188***	***1.199***		
Officer	Ranch Hand	319	1.157	–0.037 --	0.590
	Comparison	457	1.194		
Enlisted Flyer	Ranch Hand	139	1.289	0.040 --	0.719
	Comparison	179	1.249		
Enlisted Groundcrew	Ranch Hand	365	1.177	0.028 --	0.668
	Comparison	552	1.149		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	148	1.305	1.288	0.037	–0.071 (0.027)	0.010
Medium	154	1.037	1.036			
High	156	0.979	0.992			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of PSA versus $\log_2$ (initial dioxin).

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

Table 10-35. Analysis of PSA (ng/ml) (Continuous) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	147	0.975	0.114	–0.045 (0.031)	0.152
Medium	154	0.806			
High	154	0.811			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of PSA versus log_2 (initial dioxin).

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,152	1.125	1.127		
Background RH	365	1.118	1.099	–0.028 --	0.587
Low RH	222	1.199	1.205	0.078 --	0.227
High RH	236	1.006	1.023	–0.104 --	0.079
Low plus High RH	458	1.095	1.108	–0.019 --	0.692

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 10-35. Analysis of PSA (ng/ml) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,151	1.201		
Background RH	362	1.163	–0.038 --	0.527
Low RH	221	1.258	0.057 --	0.441
High RH	234	1.209	0.008 --	0.919
Low plus High RH	455	1.232	0.031 --	0.600

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	276	1.133	0.005	–0.037 (0.018)	0.043
Medium	268	1.192			
High	279	1.003			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of PSA versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	275	1.111	0.076	–0.021 (0.020)	0.312
Medium	265	1.135			
High	277	1.033			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of PSA versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

The unadjusted Model 2 analysis revealed a significant inverse association between initial dioxin and continuous PSA (Table 10-35(c): slope=–0.071, p=0.010). After adjustment for covariates, the association was nonsignificant (Table 10-35(d): p=0.152).

A marginally significant difference in mean continuous PSA levels was found between Ranch Hands in the high dioxin category and Comparisons in the Model 3 unadjusted analysis (Table 10-35(e): difference of means=–0.104, p=0.079). After adjustment for covariates, the difference was nonsignificant (Table 10-35(f): p=0.919). All other Model 3 contrasts were also nonsignificant (Table 10-35(e,f): p>0.22).

A significant inverse association between 1987 dioxin and continuous PSA levels was revealed from the unadjusted Model 4 analysis (Table 10-35(g): adjusted slope=–0.037, p=0.043). After adjustment for covariates, the association was nonsignificant (Table 10-35(h): p=0.312).

10.2.2.2.2 PSA (Discrete)

A marginally significant difference in the percentage of participants with abnormally high PSA levels between Ranch Hand and Comparison officers was found in the Model 1 unadjusted analysis (Table 10-36(a): Est. RR=1.59, p=0.086). After adjustment for covariates, the contrast was nonsignificant (Table 10-36(b): p=0.216). All other Model 1 contrasts were nonsignificant (Table 10-36(a,b): p>0.21).

Table 10-36. Analysis of PSA (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***829***	***54 (6.5)***	***1.07 (0.74,1.53)***	***0.730***
	Comparison	***1,190***	***73 (6.1)***		
Officer	Ranch Hand	320	31 (9.7)	1.59 (0.94,2.69)	0.086
	Comparison	458	29 (6.3)		
Enlisted Flyer	Ranch Hand	141	10 (7.1)	0.84 (0.37,1.93)	0.681
	Comparison	180	15 (8.3)		
Enlisted Groundcrew	Ranch Hand	368	13 (3.5)	0.66 (0.34,1.29)	0.223
	Comparison	552	29 (5.3)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.02 (0.64,1.60)***	***0.947***
Officer	1.45 (0.80,2.63)	0.216
Enlisted Flyer	0.78 (0.32,1.90)	0.578
Enlisted Groundcrew	0.68 (0.33,1.41)	0.302

Table 10-36. Analysis of PSA (Discrete) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	148	19 (12.8)	0.53 (0.37,0.77)	<0.001
Medium	154	13 (8.4)		
High	156	2 (1.3)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
455	0.61 (0.40,0.93)	0.014

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,152	71 (6.2)		
Background RH	365	20 (5.5)	0.85 (0.51,1.42)	0.526
Low RH	222	22 (9.9)	1.69 (1.02,2.79)	0.040
High RH	236	12 (5.1)	0.85 (0.45,1.59)	0.603
Low plus High RH	458	34 (7.4)	1.18 (0.76,1.84)	0.454

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 10-36. Analysis of PSA (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,151		
Background RH	362	0.76 (0.43,1.37)	0.368
Low RH	221	1.42 (0.79,2.56)	0.246
High RH	234	1.04 (0.51,2.16)	0.907
Low plus High RH	455	1.21 (0.71,2.08)	0.484

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	276	15 (5.4)	0.91 (0.75,1.10)	0.313
Medium	268	26 (9.7)		
High	279	13 (4.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
817	1.05 (0.81,1.35)	0.735

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

The Model 2 unadjusted and adjusted analyses of discrete PSA revealed a significant inverse relation between initial dioxin and discrete PSA levels (Table 10-36(c,d): Est. RR=0.53, p<0.001; Adj. RR=0.61, p=0.014, respectively). As initial dioxin in Ranch Hands increased, the prevalence of abnormally high PSA levels decreased.

A significant difference in the percentage of Ranch Hands in the low dioxin category with abnormally high PSA levels and Comparisons was observed in the unadjusted Model 3 analysis (Table 10-36(e): Est. RR=1.69, p=0.040). After adjustment for covariates, the result was nonsignificant (Table 10-36(f):

p=0.246). All other Model 3 analysis results, as well as Model 4 results, were also nonsignificant (Table 10-36(e-h): p>0.31 for each).

10.2.3 Longitudinal Analysis

Longitudinal analyses were conducted on three variables—malignant skin neoplasms, malignant systemic neoplasms, and benign systemic neoplasms—to examine whether changes across time differed with respect to group membership (Model 1), initial dioxin (Model 2), and categorized dioxin (Model 3). Model 4 was not examined in longitudinal analyses because 1987 dioxin, the measure of exposure in these models, changes over time and is not available for all participants for 1982 or 1997.

The longitudinal analyses for all of these variables investigated the difference between the 1982 examination and the 1997 examination. These analyses were used to investigate the temporal effects of herbicide or dioxin exposure during the 15-year period between 1982 and 1997. Participants who were abnormal in 1982 were not included in the analyses. The purpose of the longitudinal analysis was to examine the effects of dioxin exposure across time. Participants who were abnormal in 1982 were not considered to be at risk for developing neoplasms, because the condition already existed at the time of the first collection of data for the AFHS (1982). Only participants considered normal at the 1982 examination (i.e., no neoplasm) were considered to be at risk when the effects of herbicide or dioxin exposure over this period of time were explored; therefore, the rate of abnormalities under this restriction approximates an incidence rate between 1982 and 1997. That is, an incidence rate is a measure of the rate at which people without a condition develop the condition during a specified period of time (81). Summary statistics are provided for reference purposes for the 1985, 1987, and 1992 examinations. All three models were adjusted for age; Models 2 and 3 also were adjusted for the percentage of body fat at the time of the blood measurement of dioxin.

10.2.3.1 Medical Records Review

10.2.3.1.1 Malignant Skin Neoplasms

The longitudinal analysis results for participants with no malignant skin neoplasms in 1982 were nonsignificant for Models 1, 2, and 3 (Table 10-37(a-c): p>0.31 for each analysis).

Table 10-37. Longitudinal Analysis of Malignant Skin Neoplasms

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) Yes/(n) Examination 1982	1985	1987	1992	1997
All	***Ranch Hand***	***41 (5.1) (809)***	***62 (7.8) (791)***	***82 (10.5) (783)***	***114 (14.5) (788)***	***137 (16.9) (809)***
	Comparison	***31 (3.2) (967)***	***60 (6.3) (949)***	***70 (7.4) (942)***	***113 (11.9) (948)***	***157 (16.2) (967)***
Officer	Ranch Hand	21 (6.8) (307)	33 (10.9) (303)	44 (14.7) (300)	61 (20.1) (303)	71 (23.1) (307)
	Comparison	15 (4.0) (374)	31 (8.4) (368)	36 (9.9) (362)	64 (17.3) (370)	83 (22.2) (374)
Enlisted Flyer	Ranch Hand	9 (6.1) (147)	12 (8.3) (144)	16 (11.3) (142)	24 (16.7) (144)	29 (19.7) (147)
	Comparison	3 (2.1) (144)	7 (4.9) (143)	9 (6.3) (142)	15 (10.6) (142)	19 (13.2) (144)
Enlisted Groundcrew	Ranch Hand	11 (3.1) (355)	17 (4.9) (344)	22 (6.5) (341)	29 (8.5) (341)	37 (10.4) (355)
	Comparison	13 (2.9) (449)	22 (5.0) (438)	25 (5.7) (438)	34 (7.8) (436)	55 (12.3) (449)

Occupational Category	Group	No in 1982: n in 1997	No in 1982: Number (%) Yes in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***768***	***96 (12.5)***	***0.92 (0.69,1.23)***	***0.594***
	Comparison	***936***	***126 (13.5)***		
Officer	Ranch Hand	286	50 (17.5)	0.90 (0.60,1.36)	0.628
	Comparison	359	68 (18.9)		
Enlisted Flyer	Ranch Hand	138	20 (14.5)	1.33 (0.66,2.70)	0.427
	Comparison	141	16 (11.4)		
Enlisted Groundcrew	Ranch Hand	344	26 (7.6)	0.78 (0.47,1.31)	0.348
	Comparison	436	42 (9.6)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who did not have a malignant skin neoplasm in 1982 (see Chapter 7, Statistical Methods).

Table 10-37. Longitudinal Analysis of Malignant Skin Neoplasms (Continued)

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN					
	Number (%) Yes/(n) Examination				
Initial Dioxin	1982	1985	1987	1992	1997
Low	11 (7.4) (148)	19 (13.1) (145)	21 (14.3) (147)	27 (18.8) (144)	30 (20.3) (148)
Medium	9 (5.7) (158)	11 (7.1) (155)	15 (9.7) (155)	22 (14.2) (155)	30 (19.0) (158)
High	4 (2.6) (153)	6 (4.0) (150)	9 (6.1) (148)	13 (8.7) (150)	17 (11.1) (153)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	No in 1982			
Initial Dioxin	n in 1997	Number (%) Yes in 1997	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	137	19 (13.9)	0.88 (0.69,1.13)	0.313
Medium	149	21 (14.1)		
High	149	13 (8.7)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Notes: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who did not have a malignant skin neoplasm in 1982 (see Chapter 7, Statistical Methods).

Table 10-37. Longitudinal Analysis of Malignant Skin Neoplasms (Continued)

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY					
	Number (%) Yes/(n) Examination				
Dioxin Category	1982	1985	1987	1992	1997
Comparison	29 (3.1) (939)	58 (6.3) (924)	67 (7.3) (916)	108 (11.7) (921)	151 (16.1) (939)
Background RH	17 (4.9) (344)	26 (7.7) (336)	37 (11.3) (328)	52 (15.6) (334)	60 (17.4) (344)
Low RH	17 (7.6) (224)	26 (11.9) (218)	28 (12.7) (221)	40 (18.4) (218)	46 (20.5) (224)
High RH	7 (3.0) (235)	10 (4.3) (232)	17 (7.4) (229)	22 (9.5) (231)	31 (13.2) (235)
Low plus High RH	24 (5.2) (459)	36 (8.0) (450)	45 (10.0) (450)	62 (13.8) (449)	77 (16.8) (459)

	No in 1982			
Dioxin Category	n in 1997	Number (%) Yes in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	910	122 (13.4)		
Background RH	327	43 (13.2)	0.94 (0.65,1.38)	0.770
Low RH	207	29 (14.0)	0.98 (0.63,1.53)	0.936
High RH	228	24 (10.5)	0.87 (0.54,1.40)	0.571
Low plus High RH	435	53 (12.2)	0.92 (0.65,1.31)	0.655

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

Notes: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who did not have a malignant skin neoplasm in 1982 (see Chapter 7, Statistical Methods).

10.2.3.1.2 Malignant Systemic Neoplasms

For participants with no malignant systemic neoplasms in 1982, differences between Ranch Hands and Comparisons examined within the enlisted flyer stratum were marginally significant (Table 10-38(a): Adj. RR=2.43, p=0.062). The percentage of participants who developed a malignant systemic neoplasm after 1982 was higher for Ranch Hand enlisted flyers than for Comparison enlisted flyers (11.0% vs. 4.8%, respectively). All other Model 1 contrasts were nonsignificant (Table 10-38(a): p>0.11).

Table 10-38. Longitudinal Analysis of Malignant Systemic Neoplasms

(a) MODEL 1: RANCH HANDS VS. COMPARISONS						
		Number (%) Yes/(n) Examination				
Occupational Category	Group	1982	1985	1987	1992	1997
All	***Ranch Hand***	***7 (0.9) (810)***	***13 (1.6) (792)***	***19 (2.4) (784)***	***31 (3.9) (788)***	***63 (7.8) (810)***
	Comparison	***10 (1.0) (974)***	***13 (1.4) (956)***	***16 (1.7) (949)***	***32 (3.4) (954)***	***62 (6.4) (974)***
Officer	Ranch Hand	4 (1.3) (306)	8 (2.7) (302)	11 (3.7) (299)	15 (5.0) (301)	31 (10.1) (306)
	Comparison	5 (1.3) (380)	8 (2.1) (374)	9 (2.5) (368)	19 (5.1) (375)	36 (9.5) (380)
Enlisted Flyer	Ranch Hand	1 (0.7) (146)	2 (1.4) (143)	2 (1.4) (141)	8 (5.6) (143)	17 (11.6) (146)
	Comparison	0 (0.0) (145)	0 (0.0) (144)	1 (0.7) (143)	4 (2.8) (143)	7 (4.8) (145)
Enlisted Groundcrew	Ranch Hand	2 (0.6) (358)	3 (0.9) (347)	6 (1.7) (344)	8 (2.3) (344)	15 (4.2) (358)
	Comparison	5 (1.1) (449)	5 (1.1) (438)	6 (1.4) (438)	9 (2.1) (436)	19 (4.2) (449)

		No in 1982			
Occupational Category	Group	n in 1997	Number (%) Yes in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***803***	***56 (7.0)***	***1.38 (0.92,2.06)***	***0.118***
	Comparison	***964***	***52 (5.4)***		
Officer	Ranch Hand	302	27 (8.9)	1.11 (0.64,1.93)	0.716
	Comparison	375	31 (8.3)		
Enlisted Flyer	Ranch Hand	145	16 (11.0)	2.43 (0.96,6.19)	0.062
	Comparison	145	7 (4.8)		
Enlisted Groundcrew	Ranch Hand	356	13 (3.7)	1.30 (0.59,2.87)	0.509
	Comparison	444	14 (3.2)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who did not have a malignant systemic neoplasm in 1982 (see Chapter 7, Statistical Methods).

Table 10-38. Longitudinal Analysis of Malignant Systemic Neoplasms (Continued)

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN					
	Number (%) Yes/(n) Examination				
Initial Dioxin	1982	1985	1987	1992	1997
Low	1 (0.7) (150)	2 (1.4) (147)	5 (3.4) (149)	7 (4.8) (145)	19 (12.7) (150)
Medium	4 (2.5) (158)	7 (4.5) (155)	7 (4.5) (155)	13 (8.4) (155)	19 (12.0) (158)
High	0 (0.0) (152)	0 (0.0) (149)	0 (0.0) (147)	0 (0.0) (149)	5 (3.3) (152)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	No in 1982			
Initial Dioxin	n in 1997	Number (%) Yes in 1997	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	149	18 (12.1)	0.71 (0.50,1.00)	0.036
Medium	154	15 (9.7)		
High	152	5 (3.3)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who did not have a malignant systemic neoplasm in 1982 (see Chapter 7, Statistical Methods).

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY					
	Number (%) Yes/(n) Examination				
Dioxin Category	1982	1985	1987	1992	1997
Comparison	10 (1.1) (946)	13 (1.4) (931)	16 (1.7) (923)	31 (3.3) (927)	61 (6.5) (946)
Background RH	2 (0.6) (344)	4 (1.2) (336)	7 (2.1) (328)	11 (3.3) (334)	20 (5.8) (344)
Low RH	3 (1.3) (225)	6 (2.7) (219)	9 (4.1) (222)	16 (7.3) (218)	33 (14.7) (225)
High RH	2 (0.9) (235)	3 (1.3) (232)	3 (1.3) (229)	4 (1.7) (231)	10 (4.3) (235)
Low plus High RH	5 (1.1) (460)	9 (2.0) (451)	12 (2.7) (451)	20 (4.5) (449)	43 (9.4) (460)

Table 10-38. Longitudinal Analysis of Malignant Systemic Neoplasms (Continued)

Dioxin Category	No in 1982: n in 1997	No in 1982: Number (%) Yes in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	936	51 (5.5)		
Background RH	342	18 (5.3)	0.89 (0.50,1.57)	0.687
Low RH	222	30 (13.5)	2.58 (1.57,4.25)	<0.001
High RH	233	8 (3.4)	0.88 (0.40,1.91)	0.740
Low plus High RH	455	38 (8.4)	1.48 (0.89,2.48)	0.132

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who did not have a malignant systemic neoplasm in 1982 (see Chapter 7, Statistical Methods).

The Model 2 longitudinal analysis revealed a significant inverse association between initial dioxin and malignant systemic neoplasms after 1982 (Table 10-38(b): Adj. RR=0.71, p=0.036). The percentage of Ranch Hands at the 1997 follow-up examination with a malignant systemic neoplasm since 1982 decreased as initial dioxin levels increased.

A significantly higher percentage of malignant systemic neoplasms in Ranch Hands in the low dioxin category than Comparisons was found from the Model 3 analysis (Table 10-38(c): Adj. RR=2.58, p<0.001). All other Model 3 longitudinal contrasts were nonsignificant (Table 10-38(c): p>0.13).

10.2.3.1.3 Benign Systemic Neoplasms

All longitudinal analysis results for a history of benign systemic neoplasms since 1982 were nonsignificant for Models 1, 2, and 3 (Table 10-39(a-c): p>0.11).

Table 10-39. Longitudinal Analysis of Benign Systemic Neoplasms

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) Yes/(n) Examination 1982	1985	1987	1992	1997
All	***Ranch Hand***	***44 (5.4) (810)***	***69 (8.7) (792)***	***111 (14.2) (784)***	***145 (18.4) (788)***	***213 (26.3) (810)***
	Comparison	***69 (7.1) (974)***	***98 (10.3) (956)***	***132 (13.9) (949)***	***178 (18.7) (954)***	***259 (26.6) (974)***
Officer	Ranch Hand	19 (6.2) (306)	27 (8.9) (302)	45 (15.1) (299)	53 (17.6) (301)	81 (26.5) (306)
	Comparison	35 (9.2) (380)	46 (12.3) (374)	56 (15.2) (368)	74 (19.7) (375)	115 (30.3) (380)
Enlisted Flyer	Ranch Hand	10 (6.9) (146)	14 (9.8) (143)	24 (17.0) (141)	33 (23.1) (143)	42 (28.8) (146)
	Comparison	8 (5.5) (145)	12 (8.3) (144)	24 (16.8) (143)	30 (21.0) (143)	40 (27.6) (145)
Enlisted Groundcrew	Ranch Hand	15 (4.2) (358)	28 (8.1) (347)	42 (12.2) (344)	59 (17.2) (344)	90 (25.1) (358)
	Comparison	26 (5.8) (449)	40 (9.1) (438)	52 (11.9) (438)	74 (17.0) (436)	104 (23.2) (449)

Occupational Category	Group	No in 1982: n in 1997	No in 1982: Number (%) Yes in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***766***	***169 (22.1)***	***1.07 (0.84,1.35)***	***0.585***
	Comparison	***905***	***190 (21.0)***		
Officer	Ranch Hand	287	62 (21.6)	0.90 (0.62,1.32)	0.601
	Comparison	345	80 (23.2)		
Enlisted Flyer	Ranch Hand	136	32 (23.5)	1.02 (0.58,1.78)	0.953
	Comparison	137	32 (23.4)		
Enlisted Groundcrew	Ranch Hand	343	75 (21.9)	1.26 (0.88,1.80)	0.202
	Comparison	423	78 (18.4)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who did not have a benign systemic neoplasm in 1982 (see Chapter 7, Statistical Methods).

Table 10-39. Longitudinal Analysis of Benign Systemic Neoplasms (Continued)

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN

Initial Dioxin	Number (%) Yes/(n) Examination 1982	1985	1987	1992	1997
Low	11 (7.3) (150)	15 (10.2) (147)	24 (16.1) (149)	25 (17.2) (145)	41 (27.3) (150)
Medium	11 (7.0) (158)	16 (10.3) (155)	18 (11.6) (155)	27 (17.4) (155)	38 (24.1) (158)
High	5 (3.3) (152)	14 (9.4) (149)	20 (13.6) (147)	27 (18.1) (149)	42 (27.6) (152)

Initial Dioxin Category Summary Statistics: Initial Dioxin	No in 1982: n in 1997	Number (%) Yes in 1997	Analysis Results for Log_2 (Initial Dioxin)[a]: Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	139	30 (21.6)	1.16 (0.97,1.38)	0.114
Medium	147	27 (18.4)		
High	147	37 (25.2)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Notes: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who did not have a benign systemic neoplasm in 1982 (see Chapter 7, Statistical Methods).

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY

Dioxin Category	Number (%) Yes/(n) Examination 1982	1985	1987	1992	1997
Comparison	66 (7.0) (946)	95 (10.2) (931)	128 (13.9) (923)	172 (18.6) (927)	251 (26.5) (946)
Background RH	17 (4.9) (344)	24 (7.1) (336)	48 (14.6) (328)	65 (19.5) (334)	90 (26.2) (344)
Low RH	17 (7.6) (225)	25 (11.4) (219)	34 (15.3) (222)	37 (17.0) (218)	57 (25.3) (225)
High RH	10 (4.3) (235)	20 (8.6) (232)	28 (12.2) (229)	42 (18.2) (231)	64 (27.2) (235)
Low plus High RH	27 (5.9) (460)	45 (10.0) (451)	62 (13.8) (451)	79 (17.6) (449)	121 (26.3) (460)

Table 10-39. Longitudinal Analysis of Benign Systemic Neoplasms (Continued)

Dioxin Category	No in 1982: n in 1997	No in 1982: Number (%) Yes in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	880	185 (21.0)		
Background RH	327	73 (22.3)	1.05 (0.77,1.43)	0.754
Low RH	208	40 (19.2)	0.85 (0.58,1.25)	0.413
High RH	225	54 (24.0)	1.30 (0.91,1.85)	0.144
Low plus High RH	433	94 (21.7)	1.06 (0.80,1.41)	0.679

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who did not have a benign systemic neoplasm in 1982 (see Chapter 7, Statistical Methods).

10.3 DISCUSSION

In ambulatory medicine, the recommendation that asymptomatic individuals undergo periodic physical examinations is based largely on the assumption that such screening may reveal occult malignancy. Although the guidelines for the frequency and content of such examinations are subject to debate, there is no doubt that early detection affords the best and, in most forms of cancer, the only chance for cure. While no one screening test is absolutely reliable, the scope and depth of the protocol employed in this longitudinal study far exceed that considered routine in clinical practice.

As the anatomic point of contact with industrial toxins and as the only organ system with a clearly defined clinical endpoint (i.e., chloracne) for dioxin exposure, the skin deserves the special emphasis it has received in this study. Although there is no evidence that dioxin exposure causes—or that chloracne is associated with—basal cell carcinomas, the Ranch Hand cohort was found to be at increased risk for the occurrence of these skin cancers in the 1982, 1985, 1987, and 1992 AFHS examinations. As in previous examinations, skin lesions considered to be suggestive of skin cancer were biopsied. Although blind to the participant exposure status, examiners performed a similar number of biopsies in the Ranch Hand (54 out of 869, or 6.2%) and Comparison (68 out of 1,251, or 5.4%) cohorts.

Consistent with each of the preceding examinations, Ranch Hands continued to have a slightly higher history of benign and malignant skin neoplasms than Comparisons, including that of basal cell skin cancers at all sites (15.0% of Ranch Hands vs. 13.3% of Comparisons). In neither the current nor the 1992 examination were the group differences significant. Further, although the statistical significance varied, in all of the exposure analyses employing initial and 1987 serum dioxin levels, an inverse dose-response relation was documented with basal cell skin cancers decreasing as the level of serum dioxin

increased. The current results are consistent with results of the exposure analyses from both the 1987 and 1992 examinations. Once again, although group differences were not statistically significant, cutaneous melanoma and squamous cell skin cancers were greater in Ranch Hands than in Comparisons.

In the 1987 examination, one of the few statistically significant findings was an increase of benign systemic neoplasms in the Ranch Hand cohort relative to Comparisons (10.2% vs. 4.1%) in a pattern consistent with a dose-response effect. In the 1992 and 1997 examinations, the occurrence of benign systemic neoplasms was close to equal in both cohorts (16.4% vs. 15.6% and 25.4% vs. 24.1%, respectively), and in neither study did the exposure analyses reveal any association with either initial or 1987 serum dioxin levels.

Consistent with all previous examinations, the overall history of systemic malignancies at all sites combined was similar in the Ranch Hand and Comparison cohorts. In two specific diagnostic categories, statistically significant group differences were noted to the adverse effect of Ranch Hands. Malignancies of the kidney and bladder and of the bronchus and lung were more common in Ranch Hands than in Comparisons (1.3% vs. 0.5% and 1.2% vs. 0.2%, respectively). In neither case did the exposure analyses reveal any evidence for a dose-response effect associated with prior exposure to dioxin. Hodgkin's disease, non-Hodgkin's lymphoma, and STS, widely regarded as related to dioxin exposure, were both rare and less prevalent in Ranch Hands than in Comparisons (0.1% vs. 0.2% of each of Hodgkin's disease and non-Hodgkin's lymphoma). Five participants in the 1997 examination (two Ranch Hands and three Comparisons) had been diagnosed as having STS. One of the Ranch Hands was an officer with a dioxin level of 9.7 ppt measured in blood collected in 1987 and the other was an enlisted groundcrew member with a dioxin level of 124.9 ppt measured in blood collected in 1982. The three Comparisons were an enlisted flyer with a dioxin level of 4.9 ppt measured in blood collected in 1992, an enlisted groundcrew member with a dioxin level of 2.4 ppt measured in blood collected in 1987, and an officer with a dioxin level of 6.7 ppt measured in blood collected in 1987. An additional Ranch Hand with STS died subsequent to the 1985 AFHS physical examination and had no dioxin measurement. The prevalence of STS among participants who attended the 1997 physical is 2 out of 870 (0.23%) among Ranch Hands and 3 out of 1,251 (0.24%) among Comparisons. The prevalence of STS among all participants who were compliant to at least one examination, regardless of the presence or absence of dioxin levels (Ranch Hand n=1,111, Comparison n=1,571), is 3 out of 1,111, (0.27%) among Ranch Hands and 3 out of 1,571 (0.19%) among Comparisons (relative risk=1.41, 95% confidence interval: [0.29,6.99]).

The 1992 examination was the first to incorporate PSA into the study protocol. This diagnostic test has proven highly valuable in the early detection of silent prostate cancer. Related to development of benign enlargement of the prostate gland, with age a gradual rise in this index over time would be anticipated and was documented in current PSA levels relative to 1992. By discrete and continuous analyses, PSA levels were similar in Ranch Hands and Comparisons and prostate cancer in the two cohorts was nearly identical. Further, in all exposure analyses, there was no association between prostate cancer and either initial or 1987 serum dioxin levels.

Dependent variable-covariate associations confirm the increased risk of various systemic cancers in association with well established risk factors including age, cigarette use, and alcohol consumption. Eye and hair color, fair complexion, age, and residence in southern latitudes all contributed strongly to risk for the development of basal cell skin cancers. Cigarette use and alcohol consumption were strongly associated with the occurrence of bladder and lung cancer. A significant increase in prostate and basal cell skin cancers was noted in officers relative to the enlisted occupational strata. These findings are more likely to have a socio-economic than biologic basis and may reflect more frequent dermatological examinations and PSA screenings by officers relative to enlisted men.

At the end of 15 years of surveillance, Ranch Hands as a group exhibited a nonsignificant increase in the risk of malignant neoplastic disease relative to Comparisons (relative risk=1.06, 95% confidence interval: [0.80,1.41]). Contrasts by military occupation were inconsistent and, therefore, not supportive of an adverse effect of herbicide or dioxin exposure on the occurrence of malignancies. Ranch Hand enlisted groundcrew, the occupation with the highest dioxin levels and, presumably, the highest herbicide exposure, exhibited a decreased prevalence (relative risk=0.78, 95% confidence interval: [0.51,1.19]). Enlisted flyers (relative risk=1.63, 95% confidence interval: [0.91,2.92]), and officers (relative risk=1.14, 95% confidence interval: [0.79,1.65]), occupations with lower dioxin levels, exhibited nonsignificant increases in the prevalence of malignant disease. The risk of malignant disease was not significantly increased among Ranch Hands having the highest dioxin levels (relative risk=1.01, 95% confidence interval: [0.66,1.57]). Longitudinal analyses found no significant group differences with regard to the risk of malignancy and no pattern suggestive of an adverse relation between herbicide or dioxin exposure and the occurrence of malignant neoplastic disease.

10.4 SUMMARY

Skin and systemic neoplasms, verified from a medical records review, and PSA were examined in the neoplasia assessment. Each health endpoint was examined for an association with exposure group (Model 1), initial dioxin (Model 2), categorized dioxin (Model 3), and 1987 dioxin levels (Model 4). Complete adjusted analyses were limited for many of the site-specific malignant systemic neoplasms because of the sparse number of neoplasms.

10.4.1 Model 1: Group Analysis

Several significant results were observed in the Model 1 adjusted analysis of the neoplasia endpoints. Each significant result showed more Ranch Hands than Comparisons with the specific skin or systemic type neoplasm; however, no significant results were found within the enlisted groundcrew stratum, the military occupational category believed to have been, on average, the most heavily exposed. Significantly more Ranch Hands than Comparisons had skin neoplasms (all types combined). This finding was true for officers and enlisted flyers, as well as all occupations combined. Ranch Hand enlisted flyers had a marginally significantly increase in malignant skin neoplasms in relation to Comparison enlisted flyers. An increase in benign skin neoplasms was observed in Ranch Hands over Comparisons, both when combining all occupations and when restricted to officers. Ranch Hand enlisted flyers exhibited an increase in basal cell carcinoma in relation to Comparison enlisted flyers. This result was primarily because of a marginally significant increase of basal cell carcinoma on the ear, face, head, or neck. Ranch Hand enlisted flyers showed an increase of nonmelanoma relative to Comparisons. This result also was primarily because of the increase in basal cell carcinoma in Ranch Hand enlisted flyers. Ranch Hands showed a marginally significant increase over Comparisons in malignant systemic neoplasms of the bronchus and lung and of the kidney and bladder. Complete results of the Model 1 analyses are shown in Table 10-40.

Table 10-40. Summary of Group Analysis (Model 1) for Neoplasia Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED All	Officer	Enlisted Flyer	Enlisted Groundcrew
Medical Records				
Any Skin Neoplasm	+0.007	+0.034	+0.040	NS
Malignant Skin Neoplasm	NS	NS	NS*	ns
Benign Skin Neoplasm	+0.010	+0.031	NS	NS
Skin Neoplasm of Uncertain Behavior or Unspecified Nature	NS	ns	ns	NS
Any Basal Cell Carcinoma	NS	NS	NS*	ns
Basal Cell Carcinoma on Eye, Ear, Face, Head, and Neck	NS	NS	NS	ns
Basal Cell Carcinoma on Trunk	NS	NS	NS	ns
Basal Cell Carcinoma on Upper Extremities	ns	NS	ns	ns
Basal Cell Carcinoma on Lower Extremities	NS	NS	--	ns
Squamous Cell Carcinoma	NS	NS	NS	NS
Nonmelanoma	NS	NS	+0.042	ns
Melanoma	NS	NS	ns	NS
Any Systemic Neoplasm	NS	ns	NS	NS
Malignant Systemic Neoplasm	NS	NS	+0.049	NS
Benign Systemic Neoplasm	NS	ns	NS	NS
Systemic Neoplasm of Uncertain Behavior or Unspecified Nature	ns	NS	ns	ns
Malignant Systemic Neoplasm of Eye, Ear, Face, Head, and Neck	NS	NS	ns	ns
Malignant Systemic Neoplasm of Oral Cavity, Pharynx, and Larynx	ns	NS	ns	ns
Malignant Systemic Neoplasm of Thymus, Heart, and Mediastinum	NS	NS	--	NS
Malignant Systemic Neoplasm of Thyroid Gland	NS	NS	--	ns
Malignant Systemic Neoplasm of Bronchus and Lung	+0.008	NS	NS	NS
Malignant Systemic Neoplasm of Liver	NS	ns	NS	NS
Malignant Systemic Neoplasm of Colon and Rectum	NS	NS	NS	ns
Malignant Systemic Neoplasm of Kidney and Bladder	+0.046	NS	NS	NS
Malignant Systemic Neoplasm of Prostate	ns	ns	NS	ns
Malignant Systemic Neoplasm of Testicles	NS	NS	NS	NS
Malignant Systemic Neoplasm of Connective and Other Soft Tissues	ns	--	NS	ns
Hodgkin's Disease	ns	ns	--	ns
Non-Hodgkin's Lymphoma	ns	ns	--	NS

Table 10-40. Summary of Group Analysis (Model 1) for Neoplasia Variables (Ranch Hands vs. Comparisons) (Continued)

Variable	UNADJUSTED All	UNADJUSTED Officer	UNADJUSTED Enlisted Flyer	UNADJUSTED Enlisted Groundcrew
Other Malignant Systemic Neoplasms of Lymphoid and Histiocytic Tissue	ns	ns	ns	NS
All Malignant Skin and Systemic Neoplasms	NS*	NS	+0.034	ns
All Skin and Systemic Neoplasms	+0.014	NS*	NS	NS
Laboratory				
Prostate-Specific Antigen (C)	ns	ns	NS	ns
Prostate-Specific Antigen (D)	NS	NS*	ns	ns

Notes: NS or ns: Not significant (p>0.10).
NS*: Marginally significant (0.05<p≤0.10).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00.
--: Analysis not performed because of the sparse number of participants with an abnormality.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes a relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Variable	ADJUSTED All	ADJUSTED Officer	ADJUSTED Enlisted Flyer	ADJUSTED Enlisted Groundcrew
Medical Records				
Any Skin Neoplasm	+0.005	+0.030	+0.040	NS
Malignant Skin Neoplasm	NS	NS	NS*	ns
Benign Skin Neoplasm	+0.011	+0.035	NS	NS
Skin Neoplasm of Uncertain Behavior or Unspecified Nature	NS	--	--	NS
Any Basal Cell Carcinoma	NS	NS	+0.046	ns
Basal Cell Carcinoma on Eye, Ear, Face, Head, and Neck	NS	NS	NS*	ns
Basal Cell Carcinoma on Trunk	NS	NS	NS	ns
Basal Cell Carcinoma on Upper Extremities	ns	ns	ns	ns
Basal Cell Carcinoma on Lower Extremities	NS	NS	--	ns
Squamous Cell Carcinoma	NS	NS	NS	NS
Nonmelanoma	NS	NS	+0.035	ns
Melanoma	NS	NS	--	NS
Any Systemic Neoplasm	ns	ns	ns	ns
Malignant Systemic Neoplasm	NS	NS	NS	ns
Benign Systemic Neoplasm	ns	ns	ns	NS
Systemic Neoplasm of Uncertain Behavior or Unspecified Nature	ns	ns	ns	ns

Table 10-40. Summary of Group Analysis (Model 1) for Neoplasia Variables (Ranch Hands vs. Comparisons) (Continued)

	ADJUSTED			
Variable	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Malignant Systemic Neoplasm of Eye, Ear, Face, Head, and Neck	ns	NS	ns	ns
Malignant Systemic Neoplasm of Oral Cavity, Pharynx, and Larynx	ns	NS	ns	ns
Malignant Systemic Neoplasm of Thymus, Heart, and Mediastinum	--	--	--	--
Malignant Systemic Neoplasm of Thyroid Gland	NS	NS	--	--
Malignant Systemic Neoplasm of Bronchus and Lung	NS*	NS	NS	--
Malignant Systemic Neoplasm of Liver	NS	--	--	NS
Malignant Systemic Neoplasm of Colon and Rectum	NS	NS	NS	ns
Malignant Systemic Neoplasm of Kidney and Bladder	NS*	NS	--	NS
Malignant Systemic Neoplasm of Prostate	ns	ns	NS	ns
Malignant Systemic Neoplasm of Testicles	--	--	--	--
Malignant Systemic Neoplasm of Connective and Other Soft Tissues	ns	--	--	--
Hodgkin's Disease	ns	ns	--	--
Non-Hodgkin's Lymphoma	ns	--	--	ns
Other Malignant Systemic Neoplasms of Lymphoid and Histiocytic Tissue	ns	ns	--	NS
All Malignant Skin and Systemic Neoplasms	NS	NS	NS	ns
All Skin and Systemic Neoplasms	NS	NS	NS	ns
Laboratory				
Prostate-Specific Antigen (C)	NS	ns	NS	NS
Prostate-Specific Antigen (D)	NS	NS	ns	ns

Notes: NS or ns: Not significant (p>0.10).
NS*: Marginally significant (0.05<p≤0.10).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00.
--: Analysis not performed because of the sparse number of participants with an abnormality.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes a relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

10.4.2 Model 2: Initial Dioxin Analysis

The Model 1 group analysis showed significant Ranch Hand increases in the history of neoplasms relative to Comparisons. In contrast, analysis of the association of initial dioxin with neoplasms within Ranch Hands showed several significant results, but all dose-response relations were inverse in nature. As initial dioxin increased, the occurrence of a neoplasm decreased. Significant inverse dose-response related to skin neoplasms included all skin neoplasms, benign skin neoplasms, basal cell carcinoma, and basal cell carcinoma on the ear, face, head, and neck. The analysis of nonmelanoma was marginally significant.

The analysis of malignant systemic neoplasms of the thyroid gland was marginally significant, but this type of neoplasm decreased as initial dioxin increased. The prevalence of high PSA levels also decreased as initial dioxin increased. Results of all Model 2 analyses are shown in Table 10-41.

Table 10-41. Summary of Initial Dioxin Analysis (Model 2) for Neoplasia Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Any Skin Neoplasm	–0.001	–0.028
Malignant Skin Neoplasm	–0.015	ns
Benign Skin Neoplasm	–0.022	–0.020
Skin Neoplasm of Uncertain Behavior or Unspecified Nature	ns	ns
Any Basal Cell Carcinoma	–<0.001	–0.014
Basal Cell Carcinoma on Eye, Ear, Face, Head, and Neck	–<0.001	–0.003
Basal Cell Carcinoma on Trunk	ns	NS
Basal Cell Carcinoma on Upper Extremities	–0.024	ns
Basal Cell Carcinoma on Lower Extremities	NS	NS
Squamous Cell Carcinoma	ns	ns
Nonmelanoma	–0.003	ns*
Melanoma	NS	NS
Any Systemic Neoplasm	ns	NS
Malignant Systemic Neoplasm	–0.001	ns
Benign Systemic Neoplasm	NS	ns
Systemic Neoplasm of Uncertain Behavior or Unspecified Nature	ns	NS
Malignant Systemic Neoplasm of Eye, Ear, Face, Head, and Neck	ns*	ns
Malignant Systemic Neoplasm of Oral Cavity, Pharynx, and Larynx	ns	NS
Malignant Systemic Neoplasm of Thymus, Heart, and Mediastinum	--	--
Malignant Systemic Neoplasm of Thyroid Gland	–0.046	ns*
Malignant Systemic Neoplasm of Bronchus and Lung	–0.030	ns
Malignant Systemic Neoplasm of Liver	NS	NS
Malignant Systemic Neoplasm of Colon and Rectum	ns	ns
Malignant Systemic Neoplasm of Kidney and Bladder	ns	NS

Table 10-41. Summary of Initial Dioxin Analysis (Model 2) for Neoplasia Variables (Ranch Hands Only) (Continued)

Variable	Unadjusted	Adjusted
Malignant Systemic Neoplasm of Prostate	–0.007	ns
Malignant Systemic Neoplasm of Testicles	ns	ns
Malignant Systemic Neoplasm of Connective and Other Soft Tissues	NS	NS
Hodgkin's Disease	--	--
Non-Hodgkin's Lymphoma	--	--
Other Malignant Systemic Neoplasms of Lymphoid and Histiocytic Tissue	--	--
All Malignant Skin and Systemic Neoplasms	–0.001	ns
All Skin and Systemic Neoplasms	–0.017	ns
Laboratory		
Prostate-Specific Antigen (C)	–0.010	ns
Prostate-Specific Antigen (D)	–<0.001	–0.014

Notes: NS or ns: Not significant ($p>0.10$).
ns*: Marginally significant ($0.05<p\leq0.10$).
C: Continuous analysis.
D: Discrete analysis.
–: Relative risk <1.00 for discrete analysis; slope negative for continuous analysis.
--: Analysis not performed because of the sparse number of Ranch Hands with an abnormality.

P-value given if $p\leq0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater. A lowercase "ns" denotes a relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

10.4.3 Model 3: Categorized Dioxin Analysis

The unadjusted analysis of the skin neoplasia variables revealed several significant results. A significant increase of Ranch Hands in the background category relative to Comparisons was seen for all skin neoplasms combined and benign skin neoplasm. Only one contrast of Ranch Hands in the high dioxin category with Comparisons exhibited a marginally significant increase (neoplasm of the liver). Most significant results showed an increase in neoplasms of Ranch Hands in the low dioxin category relative to Comparisons. Significant or marginally significant increases of skin neoplasms in Ranch Hands in the low dioxin category were seen for all skin neoplasms, malignant skin neoplasms, basal cell carcinoma (primarily eye, ear, face, head, or neck) and nonmelanoma.

Similar to the skin neoplasm analyses, most results that were significant or marginally significant for the systemic neoplasm analyses were from the contrast of Ranch Hands in the low dioxin category with Comparisons. Any malignant systemic neoplasm, a malignant systemic neoplasm of bronchus and lung, a malignant systemic neoplasm of kidney and bladder, and a malignant systemic neoplasm of testicles were increased in Ranch Hands in the low dioxin category relative to Comparisons. In addition, an increase in all malignant skin and systemic neoplasms was observed for Ranch Hands in the low dioxin category. Complete results of the Model 3 analyses are shown in Table 10-42.

Table 10-42. **Summary of Categorized Dioxin Analysis (Model 3) for Neoplasia Variables (Ranch Hands vs. Comparisons)**

Variable	UNADJUSTED Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Medical Records				
Any Skin Neoplasm	+0.001	+0.005	ns	NS
Malignant Skin Neoplasm	NS	+0.023	ns	NS
Benign Skin Neoplasm	+<0.001	NS	ns	NS
Skin Neoplasm of Uncertain Behavior or Unspecified Nature	ns	NS	NS	NS
Any Basal Cell Carcinoma	NS	+0.012	ns	NS
Basal Cell Carcinoma on Eye, Ear, Face, Head, and Neck	NS	+0.020	ns	NS
Basal Cell Carcinoma on Trunk	NS	NS	ns	NS
Basal Cell Carcinoma on Upper Extremities	ns	NS	ns	ns
Basal Cell Carcinoma on Lower Extremities	NS	NS	ns	ns
Squamous Cell Carcinoma	NS	NS	ns	NS
Nonmelanoma	NS	+0.034	ns	NS
Melanoma	NS	NS	NS	NS
Any Systemic Neoplasm	ns	NS*	NS	NS
Malignant Systemic Neoplasm	ns	+<0.001	ns	NS
Benign Systemic Neoplasm	NS	NS	NS	NS
Systemic Neoplasm of Uncertain Behavior or Unspecified Nature	NS	NS	ns	ns
Malignant Systemic Neoplasm of Eye, Ear, Face, Head, and Neck	ns	NS	ns	NS
Malignant Systemic Neoplasm of Oral Cavity, Pharynx, and Larynx	ns	NS	ns	NS
Malignant Systemic Neoplasm of Thymus, Heart, and Mediastinum	NS*	--	--	--
Malignant Systemic Neoplasm of Thyroid Gland	ns	NS*	ns	NS
Malignant Systemic Neoplasm of Bronchus and Lung	NS	+<0.001	ns	+0.003
Malignant Systemic Neoplasm of Liver	ns	ns	NS*	NS
Malignant Systemic Neoplasm of Colon and Rectum	ns	NS*	ns	NS
Malignant Systemic Neoplasm of Kidney and Bladder	NS	+0.015	NS	NS*
Malignant Systemic Neoplasm of Prostate	ns	NS	ns	ns
Malignant Systemic Neoplasm of Testicles	--	+0.024	NS	+0.034
Malignant Systemic Neoplasm of Connective and Other Soft Tissues	ns	ns	NS	NS
Hodgkin's Disease	ns	ns	ns	ns
Non-Hodgkin's Lymphoma	ns	ns	ns	ns

Table 10-42. Summary of Categorized Dioxin Analysis (Model 3) for Neoplasia Variables (Ranch Hands vs. Comparisons) (Continued)

	UNADJUSTED			
Variable	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Other Malignant Systemic Neoplasms of Lymphoid and Histiocytic Tissue	NS	ns	ns	ns
All Malignant Skin and Systemic Neoplasms	NS	+<0.001	ns	NS
All Skin and Systemic Neoplasms	+0.030	+0.007	NS	NS*
Laboratory				
Prostate-Specific Antigen (C)	ns	NS	ns*	ns
Prostate-Specific Antigen (D)	ns	+0.040	ns	NS

Notes: NS or ns: Not significant (p>0.10).
NS* or ns*: Marginally significant (0.05<p≤0.10).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00.
--: Analysis not performed because of the sparse number of participants with an abnormality.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes a relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

	ADJUSTED			
Variable	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Medical Records				
Any Skin Neoplasm	+0.004	+0.011	NS	NS*
Malignant Skin Neoplasm	NS	NS*	NS	NS
Benign Skin Neoplasm	+0.001	NS	ns	NS
Skin Neoplasm of Uncertain Behavior or Unspecified Nature	ns	NS	ns	NS
Any Basal Cell Carcinoma	NS	+0.026	ns	NS
Basal Cell Carcinoma on Eye, Ear, Face, Head, and Neck	NS	NS*	ns	NS
Basal Cell Carcinoma on Trunk	ns	NS	NS	NS
Basal Cell Carcinoma on Upper Extremities	ns	ns	ns	ns
Basal Cell Carcinoma on Lower Extremities	NS	ns	NS	ns
Squamous Cell Carcinoma	NS	NS	NS	NS
Nonmelanoma	NS	NS*	NS	NS
Melanoma	NS	NS	NS	NS*
Any Systemic Neoplasm	ns*	ns	ns	ns
Malignant Systemic Neoplasm	ns	+0.012	ns	NS
Benign Systemic Neoplasm	ns	ns	NS	ns
Systemic Neoplasm of Uncertain Behavior or Unspecified Nature	ns	ns	ns	ns

Table 10-42. Summary of Categorized Dioxin Analysis (Model 3) for Neoplasia Variables (Ranch Hands vs. Comparisons) (Continued)

Variable	ADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Malignant Systemic Neoplasm of Eye, Ear, Face, Head, and Neck	ns	NS	ns	ns
Malignant Systemic Neoplasm of Oral Cavity, Pharynx, and Larynx	ns	NS	ns	ns
Malignant Systemic Neoplasm of Thymus, Heart, and Mediastinum	--	--	--	--
Malignant Systemic Neoplasm of Thyroid Gland	--	NS	--	--
Malignant Systemic Neoplasm of Bronchus and Lung	NS	+0.008	--	--
Malignant Systemic Neoplasm of Liver	--	--	NS*	--
Malignant Systemic Neoplasm of Colon and Rectum	ns	NS	ns	NS
Malignant Systemic Neoplasm of Kidney and Bladder	NS	+0.044	NS	NS*
Malignant Systemic Neoplasm of Prostate	ns*	ns	ns	ns
Malignant Systemic Neoplasm of Testicles	--	--	--	--
Malignant Systemic Neoplasm of Connective and Other Soft Tissues	--	--	NS	--
Hodgkin's Disease	ns	--	--	--
Non-Hodgkin's Lymphoma	ns	--	--	--
Other Malignant Systemic Neoplasms of Lymphoid and Histiocytic Tissue	NS	--	--	--
All Malignant Skin and Systemic Neoplasms	ns	+0.035	NS	NS
All Skin and Systemic Neoplasms	NS	NS	ns	NS
Laboratory				
Prostate-Specific Antigen (C)	ns	NS	NS	NS
Prostate-Specific Antigen (D)	ns	NS	NS	NS

Notes: NS or ns: Not significant (p>0.10).
NS* or ns*: Marginally significant (0.05<p≤0.10).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00.
--: Analysis not performed because of the sparse number of participants with an abnormality.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes a relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

10.4.4 Model 4: 1987 Dioxin Analysis

Results from the adjusted 1987 dioxin analysis of neoplasms showed few significant results. As 1987 dioxin increased, significant increases in basal cell carcinoma on the trunk and a malignant neoplasm of the liver were found. Significant decreases with increasing levels of 1987 dioxin were found for benign skin neoplasms and a malignant neoplasm of the thymus, heart, or mediastinum. Other results that were significant in the unadjusted analysis were nonsignificant after adjustment for covariates. Results of all analyses of 1987 dioxin are provided in Table 10-43.

Table 10-43. Summary of 1987 Dioxin Analysis (Model 4) for Neoplasia Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Any Skin Neoplasm	–0.012	ns
Malignant Skin Neoplasm	ns	NS
Benign Skin Neoplasm	–0.003	–0.005
Skin Neoplasm of Uncertain Behavior or Unspecified Nature	NS	NS
Any Basal Cell Carcinoma	–0.037	ns
Basal Cell Carcinoma on Eye, Ear, Face, Head, and Neck	–0.021	ns
Basal Cell Carcinoma on Trunk	ns	+0.016
Basal Cell Carcinoma on Upper Extremities	ns	NS
Basal Cell Carcinoma on Lower Extremities	ns	ns
Squamous Cell Carcinoma	ns	NS
Nonmelanoma	ns*	NS
Melanoma	NS	NS
Any Systemic Neoplasm	NS	NS
Malignant Systemic Neoplasm	ns	NS
Benign Systemic Neoplasm	NS	NS
Systemic Neoplasm of Uncertain Behavior or Unspecified Nature	ns	NS
Malignant Systemic Neoplasm of Eye, Ear, Face, Head, and Neck	ns	NS
Malignant Systemic Neoplasm of Oral Cavity, Pharynx, and Larynx	NS	NS
Malignant Systemic Neoplasm of Thymus, Heart, and Mediastinum	–0.038	–0.017
Malignant Systemic Neoplasm of Thyroid Gland	ns	ns
Malignant Systemic Neoplasm of Bronchus and Lung	ns	NS
Malignant Systemic Neoplasm of Liver	NS*	+0.042
Malignant Systemic Neoplasm of Colon and Rectum	NS	NS
Malignant Systemic Neoplasm of Kidney and Bladder	NS	NS
Malignant Systemic Neoplasm of Prostate	ns	ns
Malignant Systemic Neoplasm of Testicles	NS	NS
Malignant Systemic Neoplasm of Connective and Other Soft Tissues	NS	NS
Hodgkin's Disease	ns	ns

Table 10-43. Summary of 1987 Dioxin Analysis (Model 4) for Neoplasia Variables (Ranch Hands Only) (Continued)

Variable	Unadjusted	Adjusted
Non-Hodgkin's Lymphoma	ns	ns
Other Malignant Systemic Neoplasms of Lymphoid and Histiocytic Tissue	ns	ns
All Malignant Skin and Systemic Neoplasms	ns	NS
All Skin and Systemic Neoplasms	ns	ns
Laboratory		
Prostate-Specific Antigen (C)	–0.043	ns
Prostate-Specific Antigen (D)	ns	NS

Notes: NS or ns: Not significant (p>0.10).
NS* or ns*: Marginally significant (0.05<p≤0.10).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00.
–: Relative risk <1.00 for discrete analysis; slope negative for continuous analysis.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater. A lowercase "ns" denotes a relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

10.5 CONCLUSION

Several analyses showed significantly more Ranch Hands than Comparisons with a history of malignant skin or systemic neoplasms; however, no significant results were found within the enlisted groundcrew stratum, the military occupational category believed to have been, on average, the most heavily exposed. When the association between initial dioxin and malignant neoplasms was examined within Ranch Hands, the neoplasm occurrence decreased as initial dioxin increased. A significant increase of malignant neoplasms for Ranch Hands in the low dioxin category relative to Comparisons was observed, but there was no such increase in Ranch Hands in the high dioxin category. In summary, at the end of 15 years of surveillance, Ranch Hands do not exhibit a significantly increased risk for neoplastic disease, nor do they show a positive dose-response relation between dioxin and malignant neoplastic conditions.

REFERENCES

1. Van Miller, J. P., J. J. Lalich, and J. R. Allen. 1977. Increased incidence of neoplasms in rats exposed to low levels of tetrachlorodibenzo-p-dioxin. *Chemosphere* 6:537-44.
2. Kociba, R. J., D. G. Keyes, J. E. Beyer, R. M. Carreon, C. E. Wade, D. A. Dittenber, R. P. Kalnins, L. E. Frauson, C. N. Park, S. D. Barnard, R. A. Hummel, and C. G. Humiston. 1978. Results of a two-year chronic toxicity and oncogenicity study of 2,3,7,8-tetrachlorodibenzo-p-dioxin in rats. *Toxicology and Applied Pharmacology* 46:279-303.
3. Toth, K., J. Sugar, S. Somfai-Relle, and J. Bence. 1978. Carcinogenic bioassay of the herbicide 2,4,5-trichlorphenoxy ethanol (TCPE) with different 2,3,7,8-tetrachlorodibenzo-p-dioxin (dioxin) content in Swiss mice. *Progress in Biochemical Pharmacology* 14:82-93.
4. National Toxicology Program. 1982. Bioassay of 2,3,7,8-tetrachlorodibenzo-p-dioxin for possible carcinogenicity (Gavage study). Technical Report Series No. 209. National Toxicology Program, Research Triangle Park, North Carolina.
5. National Toxicology Program. 1982. Carcinogenesis bioassay of 2,3,7,8-tetrachlorodibenzo-p-dioxin (CAS no. 1746-01-6) in Swiss-Webster mice (dermal study). Report 80-32, technical report series no. 201, NIH publication no. 82-1757, Research Triangle Park, North Carolina.
6. Della Porta, G., T. A. Dragani, and G. Sozzi. 1987. Carcinogenic effects of infantile and long-term 2,3,7,8-tetrachlorodibenzo-p-dioxin in the mouse. *Tumori* 73:99-107.
7. Rao, M. S., V. Subbarao, J. D. Prasad, and D. G. Scartelli. 1988. Carcinogenicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin in the Syrian golden hamster. *Carcinogenesis* 9:1677-9.
8. DiGiovanni, J., A. Viaje, D. L. Berry, T. J. Slaga, and M. R. Juchau. 1977. Tumor initiating ability of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and Aroclor 1254 in a two-stage system of mouse skin carcinogenesis. *Bulletin of Environmental Contamination and Toxicology* 18:522-57.
9. Huff, J. E. 1992. 2,3,7,8-TCDD: a potent and complete carcinogen in experimental animals. *Chemosphere* 25:173-6.
10. Johnson, E. S. 1993. Important aspects of the evidence for TCDD carcinogenicity in man. *Environmental Health Perspectives* 99:383-90.
11. Huff, J., G. Lucier, and A. Tritscher. 1994. Carcinogenicity of TCDD: experimental, mechanistic, and epidemiologic evidence. *Annual Review of Pharmacology and Toxicology* 34:343-72.
12. Poland, A., and J. C. Knutson. 1982. 2,3,7,8-tetrachlorodibenzo-p-dioxin and related halogenated aromatic hydrocarbons: Examination of the mechanisms of toxicity. *Annual Review of Pharmacology* 22:517-54.
13. Okey, A. B., D. S. Riddick, and P. A. Harper. 1994. The Ah-receptor: Mediator of toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and related compounds. *Toxicology Letters* 70:1-22.
14. Denison, M. S. 1992. Heterogeneity of rat hepatic Ah-receptor: identification of two receptor forms which differ in their biochemical properties. *Journal of Biochemical Toxicology* 7:249-56.
15. Lucier, G. W., C. J. Portier, and M. A. Gallo. 1993. Receptor mechanisms and dose-response models for the effects of dioxins. *Environmental Health Perspectives* 101:36-44.

16. Whitlock Jr., J. P. 1990. Genetic and molecular aspects of 2,3,7,8-tetrachlorodibenzo-p-dioxin action. *Annual Review of Pharmacology and Toxicology* 30:251-77.

17. Silbergeld, E. K., and T. A. Gasiewicz. 1989. Commentary: Dioxins and the Ah receptor. *American Journal of Industrial Medicine* 16:455-74.

18. Brown, M. M., T. L. McCready, and N. J. Bunce. 1992. Factors affecting the toxicity of dioxin-like toxicants: a molecular approach to risk assessment of dioxins. *Toxicology Letters* 61:141-7.

19. DeVito, M., T. Umbreit, T. Thomas, and M. Gallo. 1991. An analogy between the actions of the Ah receptor and the estrogen receptor for use in the biological basis for risk assessment of dioxin. *Banbury Report* 35 (Biological Basis for Risk Assessment of Dioxins and Related Compounds):427-40.

20. Safe, S. 1993. Development of bioassays and approaches for the risk assessment of 2,3,7,8-tetrachlorodibenzo-p-dioxin and related compounds. *Environmental Health Perspectives* 101:317-25.

21. Andersen, M., and W. Greenlee. 1991. Biological determinants of TCDD pharmacokinetics and their relation to a biologically based risk assessment. *Banbury Report* 35 (Biological Basis for Risk Assessment of Dioxins and Related Compounds):291-310.

22. Roa, V. R. 1991. Molecular mechanism of action of dioxin-implications of its carcinogenic potency estimation. *Toxic Substances Journal* 8:335-51.

23. Houk, V. N. 1992. Review of research on health effects of PCDDs and PCDFs to develop human risk assessment. *Toxic Substances Journal* 12:181-90.

24. Kimbrough, R. D. 1992. Tolerable daily intake of 2,3,7,8-tetrachlorodibenzo-p-dioxin: recent data on mechanism and animal carcinogenicity. *Toxic Substances Journal* 12:295-306.

25. Roberts, E. A., K. C. Johnson, P. A. Harper, and A. B. Okey. 1990. Characterization of the Ah receptor mediating aryl hydrocarbon hydroxylase induction in the human liver cell line Hep G2. *Archives of Biochemistry and Biophysics* 276:442-50.

26. Choi, E., D. Toscano, J. Ryan, N. Riedel, and W. J. Toscano. 1991. Dioxin induces transforming growth factor-alpha in human keratinocytes. *Journal of Biological Chemistry* 266:9591-7.

27. Waithe, W., M. Michaud, P. Harper, A. Okey, and A. Anderson. 1991. The Ah receptor, cytochrome P450IA1 mRNA induction, and aryl hydrocarbon hydroxylase in a human lymphoblastoid cell line. *Biochemical Pharmacology* 41:85-92.

28. Lorenzen, A., and A. B. Okey. 1991. Detection and characterization of Ah receptor in tissue and cells from human tonsils. *Toxicology and Applied Pharmacology* 107:203-14.

29. Wang, X., M. Santostefano, Y. Lu, and S. Safe. 1992. A comparison of the mouse versus human aryl hydrocarbon (Ah) receptor complex: effects of proteolysis. *Chemico-Biological Interactions* 85:79-93.

30. Prokipcak, R. D., C. L. Golas, D. K. Manchester, A. B. Okey, S. Safe, and T. Fujita. 1990. 7-Substituted-2,3-dichlorodibenz-p-dioxins as competitive ligands for the Ah receptor: Quantitative structure activity relationship (QSARs) and a comparison of human receptor with Ah receptor from rodents. *Chemosphere* 20:1221-8.

31. Gough, M. 1993. Dioxin: perceptions, estimates, and measures. Phantom Risk. *Scientific Inference and the Law.* K. R. Foster, D. E. Bernstein, and P. W. Huber, eds. Cambridge, Massachusetts, The MIT Press: 249-77.

32. Bailar, J. D. 1991. Editorial: How dangerous is dioxin? *New England Journal of Medicine* 423:260-2.

33. Axelson, O. 1993. Seveso: disentangling the dioxin enigma? *Epidemiology* 4:389-92.

34. Collins, J. J., J. F. Acquavella, and B. R. Friendlander. 1992. Reconciling old and new findings on dioxin. *Epidemiology* 3:65-9.

35. Fingerhut, M. A., K. Steenland, M. H. Sweeney, W. E. Halperin, L. A. Piacitelli, and D. A. Marlow. 1992. Old and new reflections on dioxin. *Epidemiology* 3:69-72.

36. Hardell, L. 1993. Human exposure to 2,3,7,8-TCDD and risk of cancer. A response. *British Journal of Cancer* 67:337-41.

37. Sinks, T. 1993. Misclassified sarcomas and confounded dioxin exposure. *Epidemiology* 4:3-6.

38. Poole, C., J. J. Collins, M. E. Strauss, G. J. Levinskas, and P. R. Conner. 1993. Potential confounding of associations involving occupational exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Epidemiology* 4:483-4.

39. Institute of Medicine. 1996. *Veterans and Agent Orange: Update 1996*. National Academy Press: Washington, D.C.

40. Wolfe, W. H., J. E. Michalek, J. C. Miner, A. Rahe, J. Silva, W. F. Thomas, W. D. Grubbs, M. B. Lustik, T. G. Karrison, R. H. Roegner, and D. E. Williams. 1990. Health status of Air Force veterans occupationally exposed to herbicides in Vietnam. I. Physical health. *Journal of the American Medical Association* 264:1824-31.

41. Thomas, W. F., W. D. Grubbs, T. G. Karrison, M. B. Lustik, R. H. Roegner, D. E. Williams, W. H. Wolfe, J. E. Michalek, J. C. Miner, and R. W. Ogershok. 1990. An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: I. 1987 followup examination results, May 1987 to January 1990. NTIS: AD A 222 573. United States Air Force School of Aerospace Medicine, Human Systems Division (AFSC), Brooks Air Force Base, Texas.

42. Thomas, T. L., and H. K. Kang. 1990. Mortality and morbidity among Army Chemical Corps Vietnam veterans: A preliminary report. *American Journal of Industrial Medicine* 18:665-73.

43. U.S. Centers for Disease Control (USCDC). 1990. The Association of Selected Cancers With Service in the U.S. Military in Vietnam. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, Center for Environmental Health and Injury Control, Agent Orange Projects, Atlanta, Georgia.

44. Grubbs, W. D., W. H. Wolfe, J. E. Michalek, D. E. Williams, M. B. Lustik, A. S. Brockman, S. C. Henderson, F. R. Burnett, R. G. Land, D. J. Osborne, V. K. Rocconi, M. E. Schreiber, J. C. Miner, G. L. Henriksen, and J. A. Swaby. 1995. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final Report. 1992 Followup Examination Results. NTIS: AD A 304 306, 304 308-16. United States Air Force School of Aerospace Medicine, Brooks Air Force Base, Texas.

45. Visintainer, P. F., M. Barone, H. McGee, and E. L. Peterson. 1995. Proportionate mortality study of Vietnam-era veterans of Michigan. *Journal of Occupational and Environmental Medicine* 37:423-8.

46. Dalager, N. A., H. K. Kang, and T. L. Thomas. 1995. Cancer mortality patterns among women who served in the military: the Vietnam experience. *Journal of Occupational and Environmental Medicine* 37:298-305.

47. Dalager, N. A., H. K. Kang, V. L. Burt, and L. Weatherbee. 1991. Non-Hodgkin's lymphoma among Vietnam veterans. *Journal of Occupational Medicine* 33:774-9.

48. Bullman, T. A., K. K. Watanabe, and H. K. Kang. 1994. Risk of testicular cancer associated with surrogate measures of Agent Orange exposure among Vietnam veterans of the Agent Orange Registry. *Annals of Epidemiology* 4:11-6.

49. Jarone, R. E., H. M. Hayes, R. N. Hoover, J. F. Rosenthal, L. M. Brown, L. M. Pottern, N. Javadpour, K. J. O'Connell, and R. E. Stutzman. 1991. Service in Vietnam and risk of testicular cancer. *Journal of the National Cancer Institute* 83:1497-9.

50. Fingerhut, M. A., W. E. Halperin, D. A. Marlow, L. A. Piacitelli, P. A. Honchar, M. H. Sweeney, A. L. Greife, P. A. Dill, K. Steenland, and A. J. Suruda. 1991. Cancer mortality in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *New England Journal of Medicine* 324:212-8.

51. Saracci, R., M. Kogenvinas, P.-A. Bertazzi, B. H. Bueno de Mesquita, D. Coggon, L. M. Green, T. Kauppinen, K. A. L'Abbè, M. Littorin, E. Lynge, J. D. Mathews, M. Neuberger, J. Osman, N. Pearce, R. Winkelmann. 1991. Cancer mortality in workers exposed to chlorophenoxy herbicides and chlorophenols. *Lancet* 338:1027-32.

52. Manz, A., J. Berger, J. H. Dwyer, D. Flesch-Janys, S. Nagel, and H. Waltsgott. 1991. Cancer mortality among workers in chemical plant contaminated with dioxin. *Lancet* 338:959-64.

53. Bueno de Mesquita, B. H., G. Doornbos, D. A. Van der Kuip, M. Kogevinas, and R. Winkelmann. 1993. Occupational exposure to phenoxy herbicides and chlorophenols and cancer mortality in the Netherlands. *American Journal of Industrial Medicine* 23:289-300.

54. Asp, S., V. Riihimaki, S. Hernberg, and E. Pukkala. 1994. Mortality and cancer morbidity of Finnish chlorophenoxy herbicide applicators: an 18-year prospective followup. *American Journal of Industrial Medicine* 26:243-53.

55. Coggon, D., B. Pannett, and P. Winter. 1991. Mortality and incidence of cancer at four factories making phenoxy herbicides. *British Journal of Industrial Medicine* 48:173-8.

56. Lynge, E. 1993. Cancer in phenoxy herbicide manufacturing workers in Denmark, 1947-87: an update. *Cancer Causes and Control* 4:261-72.

57. Kogevinas, M., T. Kauppinen, R. Winkelmann, H. Becher, P. A. Bertazzi, B. Bas, D. Coggon, D. Green, E. Johnson, M. Littorin, E. Lynge, D. A. Marlow, J. D. Mathews, M. Neuberger, T. Benn, B. Pannett, N. Pearce, and R. Saracci. 1995. Soft tissue sarcoma and non-Hodgkin's lymphoma in workers exposed to phenoxy herbicides, chlorophenols and dioxins: two nested case-control studies. *Epidemiology* 6:396-402.

58. Smith, A., D. J. Patterson, M. Warner, R. MacKenzie, and L. Needham. 1992. Serum 2,3,7,8-tetrachlorodibenzo-p-dioxin levels of New Zealand pesticide applicators and their implication for cancer hypotheses. *Journal of the National Cancer Institute* 84:104-8.

59. Flesch-Janys, D., J. Berger, P. Gurn, A. Manz, S. Nagel, H. Waltsgott, and J. H. Dwyer. 1995. Exposure to polychlorinated dioxins and furans (PCDD/F) and mortality in a cohort of workers from a herbicide-producing plant in Hamburg, Federal Republic of Germany. *American Journal of Epidemiology* 142:1165-75.

60. Bertazzi, P.-A., A. C. Pesatori, D. Consonni, A. Tironi, M. T. Landi, and C. Zocchetti. 1993. Cancer incidence in a population accidentally exposed to 2,3,7,8-tetrachlorodibenzo-para-dioxin. *Epidemiology* 4:398-406.

61. Collins, J. J., M. E. Strauss, G. J. Levinskas, and P. R. Conner. 1993. The mortality experience of workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin in a trichloropheno-process accident [see comments]. *Epidemiology* 4:7-13.

62. Pesatori, A. C., D. Consonni, A. Tironi, C. Zocchetti, A. Fini, and P. A. Bertazzi. 1993. Cancer in a young population in a dioxin-contaminated area. *International Journal of Epidemiology* 22:1010-13.

63. Zober, A., P. Messerer, and P. Huber. 1990. Thirty-four-year mortality followup of BASF employees exposed to 2,3,7,8-TCDD after the 1953 accident. *International Archives of Occupational and Environmental Health* 62:139-57.

64. Assennato, G., D. Cervino, E. A. Emmett, G. Longo, and F. Merlo. 1989. Followup of subjects who developed chloracne following TCDD exposure at Seveso. *American Journal of Industrial Medicine* 16:119-25.

65. Patterson, D. G., L. Hampton, L. C. R. Lapeza Jr., W. T. Belser, V. Green, L. Alexander, and L. L. Needham. 1987. High resolution gas chromatographic/high-resolution mass spectrometric analysis of human serum on a whole-weight and lipid basis for 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Analytical Chemistry* 59:2000-5.

66. Michalek, J. E., R. C. Tripathi, P. M. Kulkarni, and J. L. Pirkle. 1996. The reliability of the serum dioxin measurement in veterans of Operation Ranch Hand. *Journal of Exposure Analysis and Environmental Epidemiology* 6:327-38.

67. Michalek, J. E., J. L. Pirkle, S. P. Caudill, R. C. Tripathi, D. G. Patterson Jr., and L. L. Needham. 1996. Pharmacokinetics of TCDD in Veterans of Operation Ranch Hand: 10-year Followup. *Journal of Toxicology and Environmental Health* 47:209-20.

68. Piacitelli, L. A., M. H. Sweeney, M. A. Fingerhut, D. G. Patterson, W. E. Turner, L. B. Connally, K. K. Wille, and B. Tompkins. 1992. Serum levels of PCDDs and PCDFs among workers exposed to 2,3,7,8-TCDD contaminated chemicals. *Chemosphere* 25:251-4.

69. Schecter, A., H. McGee, J. Stanley, and K. Boggess. 1992. Dioxin, dibenzofuran, and PCB, including coplanar PCB levels in the blood of Vietnam veterans in the Michigan Agent Orange Study. *Chemosphere* 24:205-8.

70. Sweeney, M. H., M. A. Fingerhut, D. G. Patterson Jr., L. B. Connally, L. A. Piacitelli, J. A. Morris, A. L. Greife, R. W. Hornung, D. A. Marlow, J. E. Dugle, W. E. Halperin, and L. L. Needham. 1990. Comparison of serum levels of 2,3,7,8-TCDD in TCP production workers and in an unexposed comparison group. *Chemosphere* 20:993-1000.

71. Johnson, E. W., W. Parsons, C. R. Weinberg, D. L. Shore, J. Mathews, D. G. Patterson, and L. L. Needham. 1992. Current serum levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin in phenoxy acid herbicide applicators and characterization of historical levels. *Journal of the National Cancer Institute* 84:1648-53.

72. Ott, M. G., A. Zober, and C. Germann. 1994. Laboratory results for selected target organs in 138 individuals occupationally exposed to TCDD. *Chemosphere* 29:2423-37.

73. Pirkle, J., and V. Houk. 1992. Use of epidemiologic studies to assess human risk from exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Chemosphere* 25:1109-16.

74. Steenland, K., L. Piacitelli, J. Deddens, M. Fingerhut, and L. I. Chang. 1999. Cancer, heart disease, and diabetes in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Journal of the National Cancer Institute* Vol. 91, No. 9:779-86.

75. Suruda, A. J., E. M. Ward, and M. A. Fingerhut. 1993. Identification of soft tissue sarcoma deaths in cohorts exposed to dioxin and to chlorinated naphthalenes. *Epidemiology* 4:14-9.

76. Bertazzi, P. 1991. Long-term effects of chemical disasters. Lessons and results from Seveso. *Science of the Total Environment* 106:5-20.

77. Assennato, G., D. Cervino, E. A. Emmett, G. Longo, and F. Merlo. 1989. Followup of subjects who developed chloracne following TCDD exposure at Seveso. *American Journal of Industrial Medicine* 16:119-25.

78. Mocarelli, P., L. L. Needham, A. Marocchi, D. G. Patterson Jr., P. Brambilla, P. M. Gerthoux, L. Meazza, and V. Carreri. 1991. Serum concentrations of 2,3,7,8-tetrachlorodibenzo-p-dioxin and test results from selected residents of Seveso, Italy. *Journal of Toxicology and Environmental Health* 32:357-66.

79. Ketchum, N. S., J. E. Michalek, and J. E. Burton. 1999. Serum dioxin and cancer in veterans of Operation Ranch Hand. *American Journal of Epidemiology*. 149(7):630-9.

80. Michalek, J. E., J. L. Pirkle, S. P. Caudill, R. C. Tripathi, D. G. Patterson Jr., and L. L. Needham. 1996. Pharmacokinetics of TCDD in Veterans of Operation Ranch Hand: 10-year Followup. *Journal of Toxicology and Environmental Health* 47:209-20.

81. Mausner, J. S., and A. K. Bahn. 1974. *Epidemiology – An Introductory Text*. Philadelphia: W. B. Saunders Company.

Table of Contents

List of Tables

11 NEUROLOGICAL ASSESSMENT

11.1 INTRODUCTION

11.1.1 Background

The recent association of neurological symptoms with herbicide exposure has motivated much of the research toward the potential neurotoxicity of dioxin. Studies of industrial accidents, as discussed subsequently in this section, have demonstrated that the mixed sensorimotor neuropathy associated with extreme chlorophenol toxicity is reversible and that there is little scientific evidence to date for any chronic central or peripheral neurological disease in humans associated with low-level 2,3,7,8-tetrachlorodibenzo-p-dioxin (dioxin) exposure. Neurobehavioral endpoints in humans, the subject of intensive investigation in this and other studies of Vietnam veterans, are considered separately in Chapter 12, Psychological Assessment.

Much of the basic research in animal models has focused on neurobehavioral sequelae consequent to dichlorophenoxyacetic acid (2,4-D, a component of Agent Orange) and 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) rather than dioxin toxicity in laboratory animal experiments (1–4). In another series of studies, the neurobehavioral effects of exposure to an ester of 2,4-D were found to be rapidly reversible, and the authors proposed a cellular rather than biochemical basis for the tolerance that developed with repeated injections (5, 6).

Several studies have investigated the neurotoxic effects of dioxin in laboratory animals with inconsistent results. Rats given a high dose of dioxin (1,000 μg/kg) intraperitoneally demonstrated no apparent neurological deficits (7). The intracerebroventricular administration of dioxin proved far more toxic than the subcutaneous route in producing a wasting syndrome in rats, although specific neurological indices were not examined (8). In another study, the neuromuscular effects associated with acute lethal doses of dioxin in rats were primarily in muscle tissue rather than peripheral nerves (9).

Two experimental animal studies can be cited as more relevant to the question of dioxin-induced neurotoxicity in humans. In the first study (10), strengthened by the inclusion of electrophysiologic measurements, Wistar rats received a single intraperitoneal low dose of dioxin in one of four strengths. Electrophysiologic studies of the sciatic nerve after injection documented dose-dependent and statistically significant reductions in motor and sensory nerve conduction velocities relative to the controls. In a companion report, the same authors provide histopathologic correlations with electrophysiologic findings (11). Ten months after exposure, microscopic studies confirmed the histologic appearance of a severe peripheral neuropathy of the axonal and demyelinating type.

In humans, there is only circumstantial evidence linking 2,4-D exposure to neurotoxicity, and the arguments against a causal relation have been summarized in a review article (12). Toxic doses of 2,4-D, as much as 3,600 mg given intravenously in a single dose to a human and a cumulative dose of 16,312 mg administered over 5 weeks, induced transient neurological signs and symptoms but no long-term sequelae (13).

A host of neurological symptoms has been reported following dioxin exposure and has been grouped under the generic term of "neurasthenia." Numerous studies have been published describing neurological sequelae in populations exposed to dioxin by occupation (14–21), environmental contamination (22–26)

and industrial accidents (27–33), and in association with service in Southeast Asia (SEA) during the Vietnam War (34–40).

The 1976 chemical explosion in Seveso, Italy, has provided a basis for numerous reports on the exposed population (27–30, 32, 33), and several of these reports have included clinical and laboratory indices in the examination protocols, most of which have focused on signs and symptoms of peripheral neuropathy as primary clinical endpoints. In one study, 152 subjects with chloracne, a marker for high-level dioxin exposure, were compared with controls. An abnormality was found in only 1 of 13 neurophysiologic indices, and none of the exposed subjects were found to have a peripheral neuropathy by World Health Organization criteria (30). Other investigators who included electromyographic studies in the examination protocols reached similar conclusions (27, 29, 32), as did those studying the populations exposed consequent to uncontrolled chemical reactions that occurred in Germany in 1953 (31) and in Nitro, West Virginia, in 1949 (17).

In contrast, one occupational study of 47 railroad workers examined 6 years after a chemical spill revealed evidence, through electrophysiologic measurements, for a peripheral neuropathy in 43 of these workers. High prevalences of dystonia (53%) and tremor (78%) were documented (14). These results have not been confirmed by any other studies, and the conclusions were limited by the lack of a control group and by exposure to other chemicals.

Point-source environmental exposure to dioxin has been the focus of numerous epidemiological studies, some of which have included neurological indices in their protocols (22–26). In 1971, waste byproducts contaminated with dioxin were mixed with oils and widely sprayed for dust control in residential areas in eastern Missouri. Soil concentrations in some areas reached 2,200 parts per billion, far exceeding the highest degree of ground contamination that occurred at Seveso. Comprehensive medical evaluations of exposed and unexposed cohorts included detailed neurological examinations and, in one report (24), quantitative studies of tactile, vibratory, and thermal sensory perception. The Missouri dioxin studies have been summarized in a review article (26) and, to date, none has found any clinical evidence for central or peripheral neurological disease associated with exposure to dioxin. In the only Missouri study to relate neurological endpoints to tissue levels of dioxin (23), no associations were found between the body burden of dioxin and abnormalities in deep tendon reflexes or pain and vibratory sensation.

An epidemiological study conducted by the National Institute of Occupational Safety and Health is one of few to relate serum dioxin levels to neurological indices (20). The prevalence of peripheral neuropathy was determined in 265 workers with a mean serum dioxin level of 220 parts per trillion (ppt) 15 years after exposure and in 244 referents with a level of 7 ppt. The diagnosis of peripheral neuropathy was established by symptoms and by data collected during physical examination, electrophysiologic studies, and quantitative sensory testing. Although the study could not rule out neurological symptoms associated with acute exposure, there was no evidence for a dose-response relation between dioxin levels and peripheral neuropathy.

Few studies of Vietnam veterans have incorporated neurological data into their protocols and, with the exception of the Air Force Health Study (AFHS), none has correlated neurological indices with tissue levels of dioxin. One large-scale study of American Legion veterans who served in Vietnam found an increased incidence of reported neurobehavioral disorders among veterans who reported exposure to herbicides (34).

The Vietnam Experience Study, conducted by the United States Centers for Disease Control and Prevention, compared the health status of 2,490 Vietnam veterans with 1,972 non-Vietnam veterans (35). The study protocol included comprehensive neurological examinations, nerve conduction velocity

studies, and neurophysiologic indices of vibratory, thermal, and auditory sensation. Aside from an increased prevalence of combat-related high frequency hearing loss in a pattern consistent with prior noise exposure, no neurological abnormalities were noted in association with service in Vietnam.

In the baseline examination of the AFHS (36), an increased prevalence of abnormal Babinski reflexes was noted in Ranch Hand personnel relative to Comparisons, a finding not confirmed at the 1985 (37), 1987 (38), or 1992 (39) follow-up examinations. In the 1987 examination, Ranch Hand participants were found to have more coordination abnormalities than Comparisons, but subsequent analyses found no correlation with serum dioxin levels. A few statistically significant associations were noted but not in a pattern consistent with a dose-response effect (40). In the AFHS 1992 examination, the prevalence of neurological disease was comparable in the Ranch Hand and Comparison groups, and there was no consistent evidence for a dose-response effect with either estimated initial dioxin levels or current dioxin levels (39). In the most recent report published by the Institute of Medicine (41), the committee concluded that there is "limited/suggestive" evidence of an association between exposure to certain herbicides used in Vietnam and the development of an acute or subacute transient peripheral neuropathy.

In summary, the animal research and human epidemiological studies cited above suggest that the peripheral nervous system is a target organ for acute dioxin toxicity. Longitudinal studies suggest that the neurological signs and symptoms attributable to heavy acute exposure resolve over time and are not associated with any long-term sequelae. Exposures equivalent to those likely to have been encountered by Vietnam veterans have not been associated with persistent neurological abnormalities.

11.1.2 Summary of Previous Analyses of the Air Force Health Study

11.1.2.1 1982 Baseline Study Summary Results

The 1982 AFHS neurological assessment consisted of questionnaire, physical examination, and electromyographic data obtained by examiners and technicians who were blind to the group identity of each participant. The physical examination required an average of 30 minutes to complete. Analyses were adjusted for reported alcohol usage, exposure to insecticides and industrial chemicals, and glucose intolerance (diabetes).

Results of the questionnaire disclosed no significant group differences in reported neurological diseases. The physical examination did not reveal any statistically significant group differences in the function of the 12 cranial nerves. Peripheral nerve function was assessed by the quality of four reflexes (patellar, Achilles, biceps, and Babinski); muscle strength or bulk; and reaction to the stimuli of pinprick, light touch, and vibration. Other than a statistically significant increase ($p=0.03$) in Ranch Hand Babinski reflexes, significant group differences were not detected.

Nerve conduction velocities were obtained on the ulnar nerve above and below the elbow and the peroneal nerve. The results for each segmental measurement were nearly identical in the Ranch Hand and Comparison groups. Conduction velocity showed highly significant inverse relations to both alcohol and diabetes in almost all of the anatomic measurements. No group associations or interactions were detected with the reported exposure to industrial and degreasing chemicals and insecticides.

No significant group differences were detected in four measures of central neurological function (tremor, finger-nose coordination, modified positive Romberg sign, or abnormal gait). Alcohol usage was significantly associated with the presence of tremor, and glucose intolerance was highly correlated to abnormal balance and the presence of tremor.

11.1.2.2 1985 Follow-up Study Summary Results

The 1985 AFHS neurological examination did not include the measurements of nerve conduction velocities, but otherwise repeated the baseline examination protocol. The questionnaire maintained a historical focus on neurasthenia through five questions for the 1982-1985 interval. With this similarity in examination and questionnaire, the dependent variables of the analyses were the same as those of the baseline study.

Interval questionnaire data (1982–1985) on neurological illness, verified by medical records, revealed no significant group differences. These data were added to verified baseline examination historical information to assess possible differences in the lifetime experience of neurological disease. Again, there was no significant difference between the Ranch Hand and Comparison groups.

The neurological examination evaluated neurological integrity in three broad areas: cranial nerve function, peripheral nerve status, and central nervous system (CNS) coordination. Assessment of the 12 cranial nerves was based on the measurement of 15 variables. Two summary indices were constructed. Neither the unadjusted nor the adjusted analyses disclosed any statistically significant group differences, although two variables (speech and tongue position) were of marginal significance, with Ranch Hands faring worse than Comparisons. One of the two cranial nerve summary indices was marginally significant, again with the Ranch Hands adversely affected. In contrast to the baseline examination, there was no significant group difference in Babinski reflex. The unadjusted and adjusted analyses of peripheral nerve function, as measured by eight variables (four reflexes, three sensory determinations, and muscle mass), did not reveal significant group differences. Coordination was evaluated by four measurements and a constructed summary variable. Hand tremor was found to be of marginal significance, with Ranch Hands faring slightly worse than Comparisons. The CNS summary index showed significant adverse effects for Ranch Hands.

In a longitudinal analysis of the Romberg sign and the Babinski reflex, only the Babinski reflex revealed a significant difference between the baseline examination and the 1985 follow-up examination, with the Ranch Hands shifting from significant adverse findings at the baseline examination to nonsignificant findings at the 1985 follow-up examination.

Overall, the 1985 follow-up examination findings were similar to the baseline examination findings; however, several distinct patterns were evident from the analyses:

- Substantially fewer abnormalities were detected at the 1985 follow-up examination than at the baseline examination for almost all of the variables.
- The decrease in abnormalities was similar in both groups.
- The adjusted analyses were uniformly similar to the unadjusted analyses.
- A significant result was found for the constructed CNS summary variable, and a marginally significant result was found for the constructed cranial nerve index excluding range of motion, both in the adverse direction.
- Although statistical significance at the pre-assigned significance level of 0.05 was not achieved for any of the measurement variables, the Ranch Hand group tended to have a greater percentage of abnormalities.

In conclusion, none of the 27 neurological variables demonstrated a significant group difference, although several showed an aggregation of abnormalities in the Ranch Hand group, which emphasized the need for continued surveillance. Historical reporting of neurological disease was similar in both

groups. The longitudinal analyses disclosed a reversal of significant increase in Babinski reflex abnormalities at the baseline examination to nonsignificant difference (RR=1.02) at the 1985 follow-up examination for the Ranch Hands.

11.1.2.3 1987 Follow-up Study Summary Results

The neurological health of the Ranch Hand group was not substantially different from the Comparison group. For the questionnaire variables related to neurological disease, Ranch Hands had significantly more hereditary and degenerative diseases, such as benign essential tremor. The statistical results of the group contrasts for 30 physical examination variables relating to cranial nerve function, peripheral nerve status, and CNS coordination processes generally were not significant. Unadjusted analyses disclosed marginally significantly more balance (Romberg sign) and coordination abnormalities for Ranch Hands than for Comparisons. Conversely, Ranch Hands had significantly fewer biceps reflex abnormalities than Comparisons. The longitudinal analyses for the cranial nerve index and the CNS index revealed no significant differences.

11.1.2.4 Serum Dioxin Analysis of 1987 Follow-up Study Summary Results

Overall, the neurological assessment did not indicate that dioxin was associated with neurological disease, although some analyses revealed a significant association between dioxin levels and CNS index and coordination. The adjusted analyses for the historical questionnaire variables were not significant and few statistically significant results were noted for the physical examination variables. The group contrast from the 1987 follow-up examination found that Ranch Hands had significantly more hereditary and degenerative diseases (mostly benign essential tremor) than Comparisons, but the serum dioxin analyses provided no support for the hypothesis that dioxin levels were associated with an increased risk of these diseases. The adjusted categorized current dioxin analyses for coordination found that the relative risk was significantly greater than 1.0 for Ranch Hands in the high current dioxin category. This was consistent with the previous analysis of the 1987 follow-up data, where the Ranch Hand group had significantly more coordination abnormalities than the Comparison group (1.5 percent versus 0.6 percent). The serum dioxin analyses showed significant adverse associations with the CNS index, including a marginally significant association with initial dioxin in the longitudinal analyses.

11.1.2.5 1992 Follow-up Study Summary Results

Overall, the neurological assessment found the prevalence of neurological disease to be comparable between the Ranch Hand and Comparison groups, and showed no consistent evidence of a dose-response effect with either estimated initial dioxin levels or current dioxin levels. In the group contrasts stratified by occupation, Ranch Hand enlisted groundcrew had significantly more cranial nerve index abnormalities than Comparison enlisted groundcrew. The enlisted groundcrew was the military occupation category with the highest average levels of dioxin; however, analyses of serum dioxin levels did not exhibit a dose-response trend.

11.1.3 Parameters for the 1997 Neurological Assessment

11.1.3.1 Dependent Variables

The neurological assessment was based on extensive physical examination data on cranial nerve function, peripheral nerve status, and CNS coordination processes. This information was supplemented by verified histories of neurological diseases. Participants with a positive serological test for syphilis and

participants who tested positive for the human immunodeficiency virus (HIV) were excluded from the analysis of all dependent variables.

11.1.3.1.1 Medical Records Variables

The 1997 questionnaire captured data on the occurrence of neurological disorders. Positive responses were verified by a medical records review and combined with information from the baseline examination and the 1985, 1987, and 1992 follow-up examinations. The neurological diseases and disorders were classified into four categories of the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) manual: inflammatory diseases (ICD-9-CM codes 320.0–326), hereditary and degenerative diseases (ICD-9-CM codes 330.0–337.9), peripheral disorders (ICD-9-CM codes 350.1–359.9), and other neurological disorders (ICD-9-CM codes 340–349.9). The neurological inflammatory diseases found in this study consisted of meningitis caused by bacterial infection, meningitis of unknown cause, and encephalitis of unknown cause. The majority of other neurological disorders were unspecified encephalopathies, but conditions such as multiple sclerosis, other demyelinating diseases of the CNS, hemiplegia, other paralytic syndromes, epilepsy, migraine, catalepsy or narcolepsy, other conditions of the brain, and other unspecified disorders of the CNS were included. Each of the four disorders was coded as "yes" or "no."

Participants with a verified pre-SEA history of the disorder were excluded from all analyses pertaining to that disorder.

11.1.3.1.2 Physical Examination Data

11.1.3.1.2.1 Cranial Nerve Function

The evaluation of cranial nerve function was based on the following 15 variables: smell, visual fields, light reaction, ocular movement, facial sensation, corneal reflex, jaw clench, smile, palpebral fissure, balance, gag reflex, speech, tongue position relative to midline, palate and uvula movement, and neck movement. All of these variables were scored as "normal" or "abnormal," except for jaw clench and palate and uvula movement, which were scored as "symmetric" or "deviated." For variables with left and right determinations, the two results were combined to produce a single normal or abnormal result, where normal indicated that both responses were normal, and abnormal indicated that at least one of the responses was abnormal. Abnormal speech conditions included aphasia, dysarthria, agnosia, and other speech abnormalities. Neck range of motion was coded as abnormal if there was a decreased range of motion forward or backward or to the left or right. Neck movement was evaluated by a shoulder shrug and by applying manual resistance to the cheeks to evaluate the strength of lateral rotation. No abnormal neck movements were found at the 1997 examination.

A cranial nerve index was created by combining responses for the 15 cranial nerve parameters. This index was classified as abnormal if at least one of the determinations was abnormal and was classified as normal if all of the cranial nerve parameters were normal.

11.1.3.1.2.2 Musculoskeletal and Vertebral Column Function

The examining neurologist asked each participant to move his head to the left and right, and to tilt his head forward and backward. This test assessed the musculoskeletal and vertebral column function. This neck range of motion variable was coded as abnormal if there was a decreased range of motion forward or backward or to the left or right.

11.1.3.1.2.3 Peripheral Nerve Status

Peripheral nerve status was assessed by light pinprick, light touch (cotton sticks), visual inspection of muscle mass (and palpation, if indicated), three deep tendon reflexes (patellar, Achilles, and biceps), and the Babinski reflex. In addition, four indices to assess bilateral symmetric distal sensory or sensorimotor polyneuropathy were analyzed. These indices were constructed based on testing of ankle and toe flexors, coordination, deep tendon reflexes, light touch, pinprick, vibration at the ankle, toe position, and a vibrotactile measurement of both great toes.

A vibrotactile measurement of both the left and right great toes was performed as part of a collaborative effort with the National Institute of Dental Research. A Vibratron II® device was used to measure vibrotactile threshold on both the left and right great toes. The Vibratron II® provided a noninvasive means of measuring the sensitivity to vibration of a participant's feet. Following instructions from the manufacturer, the Vibratron II® was calibrated prior to the start of the physical examinations and at the midpoint of the examination period. Participants whose great toes could be examined but who sensed no vibration were included in the analysis at a level equal to the highest recorded measurement (22.8 vibrational units [VU]) to represent an extreme loss of sensitivity to vibration. The Vibratron II® device recorded measurements in vibrational units. A transformation was used to convert the vibrational units to a standardized unit, such as microns of displacement, to facilitate comparison with other studies. The formula used in this study, as determined by the manufacturer, was

$$\text{Displacement (microns)} = 0.5 \bullet \text{VU}^2.$$

The instrument was calibrated prior to and once (at the midpoint) during the study period. The displacement measurements were transformed to the natural logarithm scale to enhance normal distribution assumptions for analysis. The left and right great toes were analyzed separately. For each great toe, the average (in log microns) of four of seven trials was determined. The four trials were those remaining after eliminating the results of the first of the seven trials and the high and low readings of the other six results following a method of limits protocol (42). The average was calculated for each participant who had four nonzero measurements, after eliminating the results of the first of the seven trials and the high and low readings of the other six results.

Pinprick and light touch were considered normal if the reaction was normal on both legs. A variable to judge muscle status was constructed using data on bulk; tone of upper and lower extremities; and the strength of distal wrist extensors, ankle and toe flexors, proximal deltoids, and hip flexors. Bulk was classified as either "normal" or "abnormal"; tone was classified as "abnormal" if there was either a decreased or increased response on either the left side, right side, or both sides. The strength of distal wrist extensors, ankle and toe flexors, proximal deltoids, and hip flexors was considered "abnormal" if either or both the left or right side was decreased. Composite muscle status was classified as "normal" if all of the components were normal on both the left and right sides and "abnormal" if at least one of the components was abnormal on either or both sides. The patellar, Achilles, and biceps reflexes were coded as "normal" if they were sluggish, active, or very active and were classified as "abnormal" if absent.

Three indices to assess polyneuropathy were based on a severity index. The endpoints discussed previously in this section assessed unilateral abnormalities, whereas these indices assessed bilateral abnormalities. These indices were considered abnormal only if both the left and right determinations were abnormal. These indices were based on the following seven conditions or sets of conditions:

- Both left and right ankle and toe flexors were abnormal (no=0, yes=1)

- The Romberg sign (equilibratory) was abnormal (no=0, yes=1)
- Both left and right Achilles reflexes were absent (no=0, yes=1)
- Reaction to a light touch was abnormal on both the left and right legs (no=0, yes=1)
- Reaction to a pinprick was abnormal on both the left and right legs (no=0, yes=1)
- Both left and right ankle vibrations were abnormal (no=0, yes=1)
- The position of both the left and right great toe was abnormal (no=0, yes=1).

A polyneuropathy severity index, which ranged from 0 to 7, was constructed as the sum of the above seven scores. The polyneuropathy severity index was classified as "mild" (index = 0, 1, or 2), "moderate" (index = 3 or 4), or "severe" (index = 5, 6, or 7). A second index, termed a polyneuropathy prevalence indicator, was coded as "abnormal" if the polyneuropathy severity index was at least 1 and "normal" if the polyneuropathy severity index was 0. A third index, termed a multiple polyneuropathy index, was coded as "abnormal" if the polyneuropathy severity index was at least 2 and "normal" if the polyneuropathy severity index was 0 or 1.

In addition, a confirmed polyneuropathy index was constructed as follows:

If at least two of the following three conditions hold,

- Both left and right Achilles reflexes were absent
- Reaction to a pinprick was abnormal on both the left and right legs
- Both left and right ankle vibrations were abnormal

and the minimum of the left and right toe averages (in log microns) was greater than 4.02, the confirmed polyneuropathy index was coded as "abnormal." If the minimum vibrotactile measurement was less than or equal to 4.02, or no more than one of the above conditions was present, the confirmed polyneuropathy index was coded as "normal." The value of 4.02 was determined by taking the minimum value of the left and right great toe average for each participant and using the 90^{th} percentile of the minimum values for Comparisons.

Participants with peripheral edema in the lower extremities were excluded from the analyses of pinprick and light touch. The analysis of the Achilles reflex excluded participants with a transient or sustained clonus in this reflex. The analysis of the patellar reflex excluded participants with a transient or sustained clonus in this reflex. Participants with peripheral edema of the lower extremities and participants with transient clonus or sustained clonus results for the Achilles reflex were excluded from the analysis of polyneuropathy indices, because pinprick, light touch, and the Achilles reflex were a component of each of the polyneuropathy indices.

11.1.3.1.2.4 CNS Coordination Processes

The evaluation of CNS coordination processes was based on the analysis of the following variables: tremor, coordination, Romberg sign, gait, and a CNS index. For these variables, multiple determinations, which include left and right as well as upper and lower responses, were combined to form a single result. A result was classified as "normal" if all determinations were normal and "abnormal" if at least one determination was abnormal. Tremor was examined for the left and right upper and lower extremities. Abnormal tremors included resting, essential, intention, and "other tremors." Coordination was a composite index defined as "normal" if the Romberg sign, finger-nose-finger and heel-knee-shin coordination processes, rapidly alternating movements of pronation and supination of hands, and rapid

patting were normal. The Romberg sign variable is equivalent to the "balance" variable analyzed as part of the cranial nerve function assessment. The gait variable was based on the examining physician's assessment of the participant's gait. An abnormal gait included conditions such as broad-based, small-stepped, ataxic, or other irregular gait patterns. A CNS index was constructed and was a composite variable based on tremor, coordination, and gait. This index was coded as "normal" if all three of the components were normal and abnormal otherwise.

11.1.3.2 Covariates

Age, race, military occupation, lifetime alcohol history, reported exposure to insecticides, reported exposure to industrial chemicals, reported exposure to degreasing chemicals, and diabetic class were covariates for all adjusted statistical analyses.

Age, race, and military occupation were determined from military records. Lifetime alcohol history was based on self-reported information from the 1997 questionnaire and combined with similar information gathered at the 1987 and 1992 follow-ups. The participants' lifetime exposures through 1992 to insecticides, industrial chemicals, and degreasing chemicals were updated with information reported in the 1997 questionnaire.

Each participant was asked about his drinking patterns throughout his lifetime. When a participant's drinking patterns changed, he was asked to describe how his alcohol consumption differed and the duration of time that the drinking pattern lasted. The participant's average daily alcohol consumption was determined for each of the reported drinking pattern periods throughout his lifetime, and an estimate of the corresponding total number of drink-years was derived. One drink-year was the equivalent of drinking 1.5 ounces of an 80-proof alcoholic beverage, one 12-ounce beer, or one 5-ounce glass of wine per day for 1 year.

In the 1997 questionnaire, a general screening question on diabetes was posed. Each participant was asked during the in-person health interview the following question: "Since the date of the last interview, has a doctor told you for the first time that you had diabetes?" All affirmative responses were verified by a medical records review and added to previously reported and verified information on diabetes from the 1982 baseline examination and the 1985, 1987, and 1992 follow-up examinations for each participant. Participants with a verified history of diabetes were combined with those participants with a 2-hour postprandial glucose level of 200 mg/dl or greater at the 1997 physical examination and classified as "diabetic" for the diabetic class covariate. Those participants without a verified history of diabetes and with a 2-hour postprandial glucose level of less than 200 mg/dl at the 1997 physical examination were classified as either "impaired" (140 mg/dl $<$2-hour postprandial glucose $<$ 200 mg/dl) or "normal" (2-hour postprandial glucose $<$140 mg/dl).

Two additional covariates based on self-reported information were used for the confirmed polyneuropathy indicator dependent variable. The 1997 questionnaire asked each study participant whether he had worked for 30 days or more with lead, mercury, chromium, nickel, copper, cadmium, manganese, arsenic, selenium, or molybdenum. Responses were combined to form a composite exposure to heavy metals covariate. The participant also was asked in the 1997 questionnaire whether he had ever worked for 30 days or more with vibrating power equipment or tools. The response (yes or no) to this question also was used as a covariate in the assessment of the confirmed polyneuropathy indicator dependent variable.

11.1.4 Statistical Methods

Table 11-1 summarizes the statistical analyses performed for the neurological assessment. The first part of Table 11-1 lists the dependent variables analyzed, data source, data form, cutpoints, covariates, and statistical methods. The second part of this table provides a further description of covariates examined. A covariate was used in its continuous form whenever possible for adjusted analyses; if the covariate was inherently discrete (e.g., military occupation), or if a categorized form was needed to develop measures of association with the dependent variables, the covariate was categorized as shown in Table 11-1.

Table 11-1. Statistical Analysis for the Neurological Assessment

Dependent Variables

Variable	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
Inflammatory Diseases	MR-V	D	Yes No	(1)	(a)	U:LR,CS A:LR
Hereditary and Degenerative Diseases	MR-V	D	Yes No	(1)	(a)	U:LR A:LR
Peripheral Disorders	MR-V	D	Yes No	(1)	(a)	U:LR A:LR
Other Neurological Disorders	MR-V	D	Yes No	(1)	(a)	U:LR A:LR
Smell	PE	D	Abnormal Normal	(1)	(b)	U:LR A:LR
Visual Fields	PE	D	Abnormal Normal	(1)	(b)	U:LR,CS A:LR
Light Reaction	PE	D	Abnormal Normal	(1)	(b)	U:LR,CS A:LR
Ocular Movement	PE	D	Abnormal Normal	(1)	(b)	U:LR A:LR
Facial Sensation	PE	D	Abnormal Normal	(1)	(b)	U:LR,CS A:LR
Corneal Reflex	PE	D	Abnormal Normal	--	--	Descriptive
Jaw Clench	PE	D	Deviated Symmetric	(1)	(b)	U:LR,CS A:LR
Smile	PE	D	Abnormal Normal	(1)	(b)	U:LR,CS A:LR
Palpebral Fissure	PE	D	Abnormal Normal	(1)	(b)	U:LR A:LR
Balance	PE	D	Abnormal Normal	(1)	(b)	U:LR,CS A:LR
Gag Reflex	PE	D	Abnormal Normal	--	--	Descriptive
Speech	PE	D	Abnormal Normal	(1)	(b)	U:LR,CS A:LR
Tongue Position Relative to Midline	PE	D	Deviated Symmetric	(1)	(b)	U:LR,CS A:LR
Palate and Uvula Movement	PE	D	Deviated Symmetric	(1)	(b)	U:LR,CS A:LR

Table 11-1. Statistical Analysis for the Neurological Assessment (Continued)

Variable	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
Cranial Nerve Index	PE	D	Abnormal Normal	(1)	(b)	U:LR A:LR L:LR
Neck Range of Motion	PE	D	Abnormal Normal	(1)	(b)	U:LR A:LR
Pinprick	PE	D	Abnormal Normal	(1)	(c)	U:LR A:LR
Light Touch	PE	D	Abnormal Normal	(1)	(c)	U:LR A:LR
Muscle Status	PE	D	Abnormal Normal	(1)	(b)	U:LR A:LR
Patellar Reflex	PE	D	Abnormal Normal	(1)	(d)	U:LR A:LR
Achilles Reflex	PE	D	Abnormal Normal	(1)	(e)	U:LR A:LR
Biceps Reflex	PE	D	Abnormal Normal	(1)	(b)	U:LR A:LR
Babinski Reflex	PE	D	Abnormal Normal	(1)	(b)	U:LR A:LR
Polyneuropathy Severity Index	PE	D	Severe Moderate None/Mild	(1)	(f)	U:PR A:PR
Polyneuropathy Prevalence Index	PE	D	Abnormal Normal	(1)	(f)	U:LR A:LR
Multiple Polyneuropathy Index	PE	D	Abnormal Normal	(1)	(f)	U:LR A:LR
Confirmed Polyneuropathy Indicator	PE	D	Abnormal Normal	(2)	(f)	U:LR,CS A:LR
Tremor	PE	D	Abnormal Normal	(1)	(b)	U:LR A:LR
Coordination	PE	D	Abnormal Normal	(1)	(b)	U:LR A:LR
Romberg Sign	PE	D	Abnormal Normal	(1)	(b)	U:LR,CS A:LR
Gait	PE	D	Abnormal Normal	(1)	(b)	U:LR A:LR
CNS Index	PE	D	Abnormal Normal	(1)	(b)	U:LR A:LR L:LR

[a]Covariates:

(1) Age, race, military occupation, lifetime alcohol history, insecticide exposure, industrial chemical exposure, degreasing chemical exposure, diabetic class.

(2) Age, race, military occupation, lifetime alcohol history, insecticide exposure, industrial chemical exposure, degreasing chemical exposure, diabetic class, composite exposure to heavy metals, worked with vibrating power equipment or tools.

Table 11-1. Statistical Analysis for the Neurological Assessment (Continued)

[b]Exclusions:

(a) Participants with positive serological tests for syphilis, participants who tested positive for HIV, participants with a verified pre-SEA history of the disorder.

(b) Participants with positive serological tests for syphilis, participants who tested positive for HIV.

(c) Participants with positive serological tests for syphilis, participants who tested positive for HIV, participants with peripheral edema of the lower extremities.

(d) Participants with positive serological tests for syphilis, participants who tested positive for HIV, participants with transient or sustained clonus of the patellar reflex.

(e) Participants with positive serological tests for syphilis, participants who tested positive for HIV, participants with transient or sustained clonus of the Achilles reflex.

(f) Participants with positive serological tests for syphilis, participants who tested positive for HIV, participants with peripheral edema of the lower extremities, participants with transient or sustained clonus of the Achilles reflex.

Covariates

Variable (units)	Data Source	Data Form	Cutpoints
Age (years)	MIL	D/C	Born ≥1942 Born <1942
Race	MIL	D	Black Non-Black
Occupation	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Lifetime Alcohol History (drink-years)	Q-SR	D/C	0 >0–40 >40
Insecticide Exposure	Q-SR	D	Yes No
Industrial Chemical Exposure	Q-SR	D	Yes No
Degreasing Chemical Exposure	Q-SR	D	Yes No
Diabetic Class	LAB/MR-V	D	• Diabetic: past history or ≥200 mg/dl 2-hr. postprandial glucose • Impaired: 140–<200 mg/dl 2-hr. postprandial glucose • Normal: <140 mg/dl 2-hr. postprandial glucose
Composite Exposure to Heavy Metals	Q-SR	D	Yes No
Worked With Vibrating Power Equipment or Tools	Q-SR	D	Yes No

Abbreviations

Data Source:
LAB: 1997 laboratory results
MIL: Air Force military records
MR-V: Medical records (verified)
PE: 1997 physical examination
Q-SR: Health questionnaire (self-reported)

Table 11-1. Statistical Analysis for the Neurological Assessment (Continued)

Data Form: D: Discrete analysis only
D/C: Appropriate form for analysis (either discrete or continuous)

Statistical Analysis: U: Unadjusted analysis
A: Adjusted analysis
L: Longitudinal analysis

Statistical Methods: CS: Chi-square contingency table analysis (continuity-adjusted)
LR: Logistic regression analysis
PR: Polytomous logistic regression analysis

Table 11-2 provides a summary of the number of participants with missing dependent variable and covariate data. In addition, the number of participants excluded because of medical conditions is given.

Table 11-2. Number of Participants Excluded or with Missing Data for the Neurological Assessment

Variable	Variable Use	Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
		Ranch Hand	Comparison	Initial	1987	Ranch Hand	Comparison
Smell	DEP	4	2	2	4	4	2
Visual Fields	DEP	0	4	0	0	0	4
Light Reaction	DEP	5	2	1	5	5	2
Facial Sensation	DEP	1	1	0	1	1	1
Corneal Reflex	DEP	7	6	5	7	7	5
Balance	DEP	0	1	0	0	0	1
Gag Reflex	DEP	1	1	0	1	1	1
Cranial Nerve Index	DEP	16	4	7	16	16	4
Muscle Status	DEP	0	1	0	0	0	1
Patellar Reflex	DEP	1	2	1	1	1	1
Achilles Reflex	DEP	0	3	0	0	0	3
Biceps Reflex	DEP	0	1	0	0	0	1
Babinski Reflex	DEP	0	3	0	0	0	3
Polyneuropathy Severity Index	DEP	0	1	0	0	0	1
Multiple Polyneuropathy Index	DEP	1	0	1	1	1	0
Confirmed Polyneuropathy Index	DEP	14	10	7	13	13	9
Coordination	DEP	0	2	0	0	0	2
Romberg Sign	DEP	0	1	0	0	0	1
CNS Index	DEP	0	1	0	0	0	1
Lifetime Alcohol History	COV	6	2	3	6	6	1
Diabetic Class	COV	9	18	5	7	7	17
Worked with Vibrating Power Equipment or Tools	COV	1	2	1	1	1	2
Composite Exposure to Heavy Metals	COV	1	0	1	1	1	0
Pre-SEA Inflammatory Diseases	EXC	0	7	0	0	0	7

Table 11-2. Number of Participants Excluded or with Missing Data for the Neurological Assessment (Continued)

Variable	Variable Use	Group: Ranch Hand	Group: Comparison	Dioxin (Ranch Hands Only): Initial	Dioxin (Ranch Hands Only): 1987	Categorized Dioxin: Ranch Hand	Categorized Dioxin: Comparison
Pre-SEA Peripheral Disorders	EXC	3	2	0	3	3	2
Pre-SEA Other Neurological Disorders	EXC	4	5	1	4	4	5
Positive Serological Test for Syphilis	EXC	1	0	0	1	1	0
HIV Positive	EXC	3	2	3	3	3	2
Peripheral Edema	EXC	45	64	26	45	45	62
Clonus – Patellar Reflex	EXC	0	1	0	0	0	1
Clonus – Achilles Reflex	EXC	1	2	0	1	1	2

Note: DEP = Dependent variable.
COV = Covariate.
EXC = Exclusion.
870 Ranch Hands and 1,251 Comparisons.
482 Ranch Hands for initial dioxin; 863 Ranch Hands for 1987 dioxin.
863 Ranch Hands and 1,213 Comparisons for categorized dioxin.

11.1.4.1 Longitudinal Analysis

The neurological longitudinal analyses were based on the cranial nerve index, excluding neck range of motion and the CNS index. Substantially fewer neurological abnormalities have been found in the 1985, 1987, 1992, and 1997 examinations than at the 1982 baseline examination, as noted in previous AFHS reports. This observation suggested that different techniques for the examination of the neurological system were used in 1982 than in the subsequent examinations. To enhance the comparability of measurements between examinations, the longitudinal assessment contrasted differences between the 1985 and 1997 neurological examinations.

11.2 RESULTS

11.2.1 Dependent Variable-Covariate Associations

The associations between the dependent variables examined in the neurological assessment and the covariates used in the adjusted analysis were investigated; the results are presented in Appendix F, Table F-3. These associations are pairwise between the dependent variable and the covariate and are not adjusted for any other covariates. Participants were excluded from each of the analyses as given in Table 11-1. Statistically significant associations are discussed below.

Age and industrial chemical exposure each exhibited significant associations with a history of hereditary and degenerative diseases (p=0.009 and p=0.022, respectively). Hereditary and degenerative diseases were greater for older participants than for younger participants (10.4% vs. 7.0%) and higher for participants reporting exposure to industrial chemicals than for those not reporting exposure (10.0% vs. 7.0%).

Tests of covariate associations with a history of peripheral disorders were significant for age ($p<0.001$), insecticide exposure ($p=0.014$), and diabetic class ($p<0.001$). Peripheral disorders were higher among older participants than younger participants (24.6% vs. 14.9%). Peripheral disorders were greater for participants exposed to insecticides (21.8%) than for participants not exposed to insecticides (16.9%), and greatest for diabetics (33.4%).

Several covariates were associated significantly with a history of other neurological disorders. Significant associations were found with age ($p<0.001$), race ($p<0.001$), occupation ($p<0.001$), industrial chemical exposure ($p<0.001$), degreasing chemical exposure ($p<0.001$), and diabetic class ($p<0.001$). Older participants had a greater history of other neurological disorders (22.0%) than did younger participants (13.4%). Blacks exhibited a greater history of other neurological disorders (33.1%) than did non-Blacks (17.3%). Other neurological disorders were highest for enlisted flyers (27.0%), followed by enlisted groundcrew (24.1%), and then by officers (8.1%). Participants reporting exposure to industrial chemicals and degreasing chemicals had more neurological disorders than participants who did not report exposure. Diabetics had the greatest history of other neurological disorders (23.9%).

Covariate association tests for the light reaction variable were significant for race ($p=0.046$). Blacks exhibited more light reaction abnormalities (2.3%) than did non-Blacks (0.5%).

Covariate association tests for smile, palpebral fissure, and balance were each significant for diabetic class ($p=0.030$, $p=0.007$, and $p=0.036$, respectively). For each variable, the most abnormalities were among diabetics, followed by those classified as normal, and then by those in the impaired diabetic category.

The neck range of motion variable was associated significantly with age ($p<0.001$), occupation ($p=0.006$), and diabetic class ($p=0.022$). A restricted range of motion was greater for older participants (22.0%) than for younger participants (9.9%). Enlisted flyers had the greatest prevalence of an abnormal neck range of motion (20.7%), followed by officers (18.1%), then enlisted groundcrew (14.0%). Diabetics displayed the highest prevalence of neck range of motion abnormalities (21.6%), followed by nondiabetics (15.6%), then by participants in the impaired diabetic category (15.4%).

Tests of covariate association for the cranial nerve index variable were significant for age ($p=0.004$) and diabetic class ($p=0.014$). An abnormal index was found in 7.5 percent of older participants and 4.4 percent of younger participants. More abnormalities were found as the level of diabetic impairment increased.

Covariate association tests were similar for the pinprick and light touch dependent variables. Each were associated significantly with age ($p=0.006$ and $p=0.022$, respectively), occupation ($p=0.006$ and $p=0.036$, respectively), and diabetic class ($p<0.001$ for both). Both variables displayed higher abnormalities among older participants, enlisted flyers, and diabetics.

The patellar reflex variable was associated significantly with age ($p<0.001$), race ($p=0.030$), and diabetic class ($p<0.001$). The higher abnormality prevalences were among older participants (4.0%, compared to 1.3% for younger participants), Blacks (6.3%, compared to 2.6% for non-Blacks), and diabetics (7.3%, compared to 2.6% for participants in the impaired category and 1.8% for nondiabetics).

Tests of covariate association for the Achilles reflex variable showed significant results for age ($p<0.001$), lifetime alcohol history ($p=0.027$), and diabetic class ($p<0.001$). Older participants had a higher prevalence of Achilles reflex abnormalities than did younger participants (22.8% vs. 9.3%). The

heaviest drinkers (in terms of drink-years) had an abnormal Achilles reflex most often (20.2%), followed by nondrinkers (18.6%), and moderate drinkers (15.4%). Achilles reflex abnormalities increased as the level of diabetic impairment increased (nondiabetic: 13.4%; impaired: 16.2%; diabetic: 31.9%).

An abnormal biceps reflex was associated significantly with diabetic class ($p=0.007$), where the prevalence of biceps reflex abnormalities increased as the level of diabetic impairment increased.

Tests of covariate association for the polyneuropathy severity index were significant for age ($p=0.002$), race ($p=0.005$), and diabetic class ($p<0.001$). Older participants displayed a greater percentage of moderate and severe index scores (2.6% and 0.4%, respectively) than younger participants (0.7% and 0.1%, respectively). Non-Blacks displayed the higher moderate index score (1.8%), while Blacks displayed the higher severe index score (1.6%). Diabetics exhibited the highest percentage of both the moderate and severe index scores (5.9% and 0.9%, respectively), followed by nondiabetics (0.9% and 0.1%, respectively). Participants in the impaired diabetic category displayed the smallest percentage of moderate and severe index scores (0.4% and 0.0%, respectively).

Covariate tests of association for the polyneuropathy prevalence index revealed significant associations with age, occupation, lifetime alcohol history, and diabetic class ($p<0.001$ for each). The percentage of abnormal polyneuropathy prevalence index results increased with age, lifetime alcohol history, and level of diabetic impairment. Enlisted flyers had the highest percentage of abnormal polyneuropathy prevalence index results (20.8%), followed by officers (16.5%), then enlisted groundcrew (12.5%).

The multiple polyneuropathy index variable was significantly associated with age ($p<0.001$), occupation ($p=0.006$), and diabetic class ($p<0.001$). The percentage of abnormal multiple polyneuropathy index findings increased with age. Enlisted flyers had the highest percentage of abnormalities (6.7%), followed by officers (4.2%), and enlisted groundcrew (2.7%). Diabetic participants had the highest prevalence of abnormal results (12.7%), followed by nondiabetics (2.4%), and participants in the impaired diabetic class (1.2%).

Age and diabetic classes were associated significantly with the confirmed polyneuropathy indicator variable ($p=0.007$ and $p<0.001$, respectively). Older participants had a higher percentage of abnormal findings than did younger participants (1.5% vs. 0.2%). Diabetic participants had the highest prevalence of confirmed polyneuropathy results (2.9%), followed by nondiabetics (0.6%), then participants in the impaired diabetic class (0.0%).

Insecticide exposure and industrial chemical exposure both were significantly associated with tremor ($p=0.003$ and $p=0.004$, respectively). Participants reporting exposure to insecticides had a higher percentage of tremors than participants who did not report exposure (8.2% vs. 4.5%). Similarly, participants reporting exposure to industrial chemicals had a higher prevalence of tremors than those who did not report exposure (8.4% vs. 5.0%).

Tests of covariate association for coordination revealed diabetic class to be significant ($p=0.013$). Abnormality rates increased as the level of diabetic impairment increased.

Diabetic class was significantly associated with Romberg sign ($p=0.036$). Diabetic participants had the highest percentage of abnormal Romberg sign results (1.7%), followed by nondiabetics (0.5%), and participants in the impaired diabetic class (0.4%).

Age and diabetic classes were associated significantly with gait ($p<0.001$ for each). Older participants had a higher percentage of an abnormal gait than did younger participants (6.8% vs. 2.8%). The prevalence of a gait abnormality increased with diabetic impairment.

Tests of covariate association for the CNS index revealed significant associations with age ($p<0.001$), insecticide exposure ($p<0.001$), and industrial chemical exposure ($p=0.021$). The percentage of participants with an abnormal index increased with age. Participants reporting exposure to insecticides had a higher percentage of abnormal CNS index results than did participants who did not report exposure (13.7% vs. 8.2%). Similarly, participants reporting exposure to industrial chemicals had a higher prevalence of abnormal results than those who did not report exposure (13.4% vs. 9.9%).

11.2.2 Exposure Analysis

The following section presents results of the statistical analysis of the dependent variables shown in Table 11-1. Dependent variables were derived from a medical records review and verification and a neurological examination to assess the cranial nerve function, peripheral nerve status, and CNS coordination processes.

Four models were examined for each dependent variable given in Table 11-1. The analyses of these models are presented below. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7, respectively. These analyses were performed both unadjusted and adjusted for relevant covariates. Model 1 examined the relation between the dependent variable and group (i.e., Ranch Hand or Comparison). In this model, exposure was defined as "yes" for Ranch Hands and "no" for Comparisons without regard to the magnitude of the exposure. As an attempt to quantify exposure, three contrasts of Ranch Hands and Comparisons were performed along with the overall Ranch Hand versus Comparison contrast. These three contrasts compared Ranch Hands and Comparisons within each occupational category (i.e., officers, enlisted flyers, and enlisted groundcrew). As described in previous reports, the average levels of exposure to dioxin were highest for enlisted groundcrew, followed by enlisted flyers, and officers.

Model 2 explored the relation between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt. If a participant did not have a 1987 dioxin level, the 1992 level was used to estimate the initial dioxin level. If a participant did not have a 1987 or a 1992 dioxin level, the 1997 level was used to estimate the initial dioxin level. A statistical adjustment for the percentage of body fat at the time of the participant's blood measurement of dioxin was included in this model to account for body-fat-related differences in elimination rate (43).

Model 3 divided the Ranch Hands examined in Model 2 into two categories based on their initial dioxin measures. These two categories are referred to as "low Ranch Hand" and "high Ranch Hand." Two additional categories, Ranch Hands with 1987 serum dioxin levels at or below 10 ppt and Comparisons with 1987 serum dioxin levels at or below 10 ppt, were formed and included in the model. Ranch Hands with 1987 serum dioxin levels at or below 10 ppt are referred to as the "background Ranch Hand" category. Dioxin levels in 1992 were used if the 1987 level was not available, and dioxin levels in 1997 were used if the 1987 and 1992 levels were not available. These four categories—Comparisons, background Ranch Hands, low Ranch Hands, and high Ranch Hands—were used in Model 3 analyses. The relation between the dependent variable in each of the three Ranch Hand categories and the dependent variable in the Comparison category was examined. A fourth contrast, exploring the relation of the dependent variable in the combined low and high Ranch Hand categories relative to Comparisons, also was conducted. This combination is referred to in the tables as the "low plus high Ranch Hand"

category. As in Model 2, a statistical adjustment for the percentage of body fat at the time of the participant's blood measurement of dioxin was included in this model.

Model 4 examined the relation between the dependent variable and 1987 lipid-adjusted dioxin levels in all Ranch Hands with a dioxin measurement. If a participant did not have a 1987 dioxin measurement, the 1992 measurement was used to determine the dioxin level. If a participant did not have a 1987 or a 1992 dioxin measurement, the 1997 measurement was used to determine the dioxin level.

11.2.2.1 Medical Records Variables

11.2.2.1.1 Inflammatory Diseases

A significant difference in the history of inflammatory diseases between Ranch Hands and Comparisons was revealed in both the unadjusted and adjusted analyses (Table 11-3(a,b): Est. RR=10.11, p=0.006; and Adj. RR=13.50, p=0.002, respectively). Seven Ranch Hands (0.8%) and one Comparison (0.1%) have had an inflammatory disease. Of the seven Ranch Hands with inflammatory diseases, three had meningitis caused by bacterial infections, three had meningitis of unknown cause, and one had encephalitis of unknown cause. The single Comparison with an inflammatory disease had encephalitis of unknown cause. All other Model 1 contrasts, as well as the Model 2 results, were nonsignificant (Table 11-3(a–d): p>0.11 for each Model 1 and Model 2 analysis).

Table 11-3. Analysis of Inflammatory Diseases

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***7 (0.8)***	***10.11 (1.24,82.35)***	***0.006***
	Comparison	***1,242***	***1 (0.1)***		
Officer	Ranch Hand	340	2 (0.6)	--	0.327[a]
	Comparison	490	0 (0.0)		
Enlisted Flyer	Ranch Hand	151	2 (1.3)	--	0.391[a]
	Comparison	185	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	375	3 (0.8)	4.56 (0.47,44.05)	0.189
	Comparison	567	1 (0.2)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a history of an inflammatory disease.

--: Results not presented because of the sparse number of participants with an inflammatory disease.

Table 11-3. Analysis of Inflammatory Diseases (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	*13.50 (1.61,113.13)*	*0.002*
Officer	--	--
Enlisted Flyer	--	--
Enlisted Groundcrew	6.38 (0.64,63.30)	0.114

--: Results not presented because of the sparse number of participants with an inflammatory disease.

Note: Results are not adjusted for race and diabetic class because of the sparse number of participants with an inflammatory disease.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	2 (1.3)	1.03 (0.48,2.18)	0.943
Medium	162	1 (0.6)		
High	157	1 (0.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
476	0.98 (0.45,2.17)	0.964

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race, occupation, industrial chemicals exposure, degreasing chemicals exposure, and diabetic class because of the sparse number of participants with an inflammatory disease.

Table 11-3. Analysis of Inflammatory Diseases (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,204	1 (0.1)		
Background RH	380	3 (0.8)	8.82 (0.91,85.93)	0.061
Low RH	239	2 (0.8)	10.31 (0.93,114.27)	0.057
High RH	240	2 (0.8)	10.86 (0.97,121.25)	0.053
Low plus High RH	479	4 (0.8)	10.58 (1.18,95.25)	0.035

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,203		
Background RH	377	13.28 (1.31,135.01)	0.029
Low RH	238	13.85 (1.20,160.07)	0.035
High RH	238	12.43 (1.03,149.42)	0.047
Low plus High RH	476	13.12 (1.39,123.67)	0.024

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for race and diabetic class because of the sparse number of participants with an inflammatory disease.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	287	2 (0.7)	0.97 (0.58,1.63)	0.920
Medium	287	3 (1.1)		
High	285	2 (0.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 11-3. Analysis of Inflammatory Diseases (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log$_2$ (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
853	0.90 (0.52,1.57)	0.716

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race and diabetic class because of the sparse number of participants with an inflammatory disease.

The Model 3 unadjusted analysis of history of inflammatory diseases revealed marginally significant differences for each contrast involving Ranch Hands in the background, low, and high dioxin categories (Table 11-3(e): Est. RR=8.82, p=0.061; Est. RR=10.31, p=0.057; and Est. RR=10.86, p=0.053, respectively). The remaining unadjusted contrast combining Ranch Hands in the low plus high dioxin category revealed significant differences between Ranch Hands and Comparisons (Table 11-3(e): Est. RR=10.58, p=0.035). Each Model 3 contrast was significant in the adjusted analysis, and each also displayed more Ranch Hands than Comparisons with inflammatory diseases (Table 10-3(f): Adj. RR=13.28, p=0.029; Adj. RR=13.85, p=0.035; Adj. RR=12.43, p=0.047; and Adj. RR=13.12, p=0.024).

Both the unadjusted and adjusted Model 4 analyses of inflammatory diseases were nonsignificant (Table 11-3(g,h): p>0.71 for each Model 4 analysis).

11.2.2.1.2 Hereditary and Degenerative Diseases

All results from Models 1 through 4 for hereditary and degenerative diseases were nonsignificant (Table 11-4(a–h): p≥0.38 for each analysis).

Table 11-4. Analysis of Hereditary and Degenerative Diseases

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***80 (9.2)***	***1.08 (0.79,1.46)***	***0.639***
	Comparison	***1,249***	***108 (8.7)***		
Officer	Ranch Hand	340	30 (8.8)	1.19 (0.72,1.97)	0.492
	Comparison	493	37 (7.5)		
Enlisted Flyer	Ranch Hand	151	19 (12.6)	1.27 (0.65,2.50)	0.484
	Comparison	187	19 (10.2)		
Enlisted Groundcrew	Ranch Hand	375	31 (8.3)	0.90 (0.56,1.43)	0.643
	Comparison	569	52 (9.1)		

Table 11-4. Analysis of Hereditary and Degenerative Diseases (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.07 (0.78,1.46)***	***0.688***
Officer	1.13 (0.68,1.89)	0.635
Enlisted Flyer	1.31 (0.66,2.62)	0.444
Enlisted Groundcrew	0.92 (0.57,1.48)	0.737

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	17 (10.6)	1.01 (0.79,1.28)	0.952
Medium	162	12 (7.4)		
High	157	14 (8.9)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
471	1.02 (0.76,1.36)	0.909

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	107 (8.8)		
Background RH	380	37 (9.7)	1.08 (0.73,1.61)	0.697
Low RH	239	21 (8.8)	1.00 (0.61,1.63)	0.999
High RH	240	22 (9.2)	1.07 (0.66,1.73)	0.792
Low plus High RH	479	43 (9.0)	1.03 (0.71,1.50)	0.864

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-4. Analysis of Hereditary and Degenerative Diseases (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,193		
Background RH	375	1.16 (0.77,1.76)	0.474
Low RH	235	0.92 (0.56,1.52)	0.736
High RH	236	1.01 (0.61,1.67)	0.979
Low plus High RH	471	0.96 (0.65,1.41)	0.841

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	287	27 (9.4)	0.96 (0.82,1.12)	0.590
Medium	287	30 (10.5)		
High	285	23 (8.1)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
846	0.92 (0.77,1.11)	0.380

[a] Relative risk for a twofold increase in 1987 dioxin.

11.2.2.1.3 Peripheral Disorders

Results from the Model 1 analysis of history of peripheral disorders displayed no significant differences between Ranch Hands and Comparisons (Table 11-5(a,b): $p>0.11$ for each unadjusted and adjusted contrast). The unadjusted and adjusted results from the Model 2 analysis also did not display a significant relation between peripheral disorders and initial dioxin (Table 11-5(c,d): $p \geq 0.40$ for the unadjusted and adjusted Model 2 analysis).

Table 11-5. Analysis of Peripheral Disorders

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***863***	***188 (21.8)***	***1.16 (0.94,1.44)***	***0.169***
	Comparison	***1,247***	***241 (19.3)***		
Officer	Ranch Hand	339	78 (23.0)	1.32 (0.94,1.85)	0.113
	Comparison	492	91 (18.5)		
Enlisted Flyer	Ranch Hand	150	36 (24.0)	1.02 (0.62,1.69)	0.941
	Comparison	186	44 (23.7)		
Enlisted Groundcrew	Ranch Hand	374	74 (19.8)	1.08 (0.77,1.50)	0.658
	Comparison	569	106 (18.6)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.12 (0.89,1.40)***	***0.341***
Officer	1.25 (0.88,1.78)	0.215
Enlisted Flyer	0.91 (0.54,1.54)	0.733
Enlisted Groundcrew	1.09 (0.77,1.54)	0.622

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	40 (25.0)	1.01 (0.86,1.18)	0.915
Medium	162	42 (25.9)		
High	157	38 (24.2)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
471	1.09 (0.90,1.32)	0.400

[a] Relative risk for a twofold increase in initial dioxin.

Table 11-5. Analysis of Peripheral Disorders (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,209	233 (19.3)		
Background RH	377	65 (17.2)	0.91 (0.67,1.23)	0.531
Low RH	239	61 (25.5)	1.42 (1.03,1.97)	0.033
High RH	240	59 (24.6)	1.32 (0.95,1.83)	0.097
Low plus High RH	479	120 (25.1)	1.37 (1.07,1.76)	0.014

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,191		
Background RH	372	0.88 (0.64,1.21)	0.437
Low RH	235	1.25 (0.89,1.76)	0.190
High RH	236	1.33 (0.94,1.90)	0.111
Low plus High RH	471	1.29 (0.99,1.69)	0.059

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	285	44 (15.4)	1.15 (1.04,1.29)	0.010
Medium	286	71 (24.8)		
High	285	70 (24.6)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 11-5. Analysis of Peripheral Disorders (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
843	1.20 (1.04,1.38)	0.011

[a] Relative risk for a twofold increase in 1987 dioxin.

The Model 3 unadjusted analysis indicated a significantly greater percentage of Ranch Hands in the low dioxin category than Comparisons with a peripheral disorder (Table 11-5(e): Est. RR=1.42, p=0.033). The result was nonsignificant after adjustment for covariates (Table 11-5(f): p=0.190). The unadjusted analysis also revealed a marginally significant increase for the Ranch Hands in the high dioxin category (Table 11-5(e): Est. RR=1.32, p=0.097). This result was nonsignificant in the adjusted analysis (Table 11-5(f): p=0.111). The contrast of Ranch Hands in the low plus high dioxin category with Comparisons displayed a significant difference in the percentage of participants with a peripheral disorder (Table 11-5(e): Est. RR=1.37, p=0.014), indicating a greater occurrence of peripheral disorders among Ranch Hands than Comparisons. The result was marginally significant after adjustment for covariates (Table 11-5(f): Adj. RR=1.29, p=0.059).

The Model 4 unadjusted and adjusted analyses each displayed a significant association between peripheral disorders and 1987 dioxin levels (Table 11-5(g): Est. RR=1.15, p=0.010; and Adj. RR=1.20, p=0.011, respectively). The occurrence of peripheral disorders increased as 1987 dioxin increased.

11.2.2.1.4 Other Neurological Disorders

A marginally significant increase in a history of other neurological disorders was found in Ranch Hands relative to Comparisons in the Model 1 analyses, both unadjusted and adjusted (Table 11-6(a,b): Est. RR=1.23, p=0.070; and Adj. RR=1.25, p=0.078). When differences were examined within each occupation, the results were nonsignificant in both the unadjusted and adjusted analyses (Table 11-6(a,b): p>0.13 for each contrast). Each Model 2 analysis also was nonsignificant (Table 11-6(c,d): p>0.48 for both analyses).

Table 11-6. Analysis of Other Neurological Disorders

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***862***	***173 (20.1)***	***1.23 (0.98,1.54)***	***0.070***
	Comparison	***1,244***	***211 (17.0)***		
Officer	Ranch Hand	338	29 (8.6)	1.12 (0.68,1.86)	0.656
	Comparison	492	38 (7.7)		
Enlisted Flyer	Ranch Hand	151	46 (30.5)	1.37 (0.85,2.22)	0.198
	Comparison	186	45 (24.2)		
Enlisted Groundcrew	Ranch Hand	373	98 (26.3)	1.22 (0.90,1.65)	0.200
	Comparison	566	128 (22.6)		

Table 11-6. Analysis of Other Neurological Disorders (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1.25 (0.98,1.59)*	*0.078*
Officer	1.09 (0.65,1.84)	0.734
Enlisted Flyer	1.33 (0.79,2.21)	0.283
Enlisted Groundcrew	1.28 (0.92,1.78)	0.136

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	34 (21.3)	1.06 (0.90,1.24)	0.483
Medium	161	41 (25.5)		
High	157	38 (24.2)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
470	0.99 (0.81,1.20)	0.922

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,206	204 (16.9)		
Background RH	377	59 (15.7)	0.88 (0.64,1.21)	0.442
Low RH	239	55 (23.0)	1.48 (1.06,2.07)	0.023
High RH	239	58 (24.3)	1.62 (1.16,2.26)	0.005
Low plus High RH	478	113 (23.6)	1.55 (1.19,2.01)	0.001

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-6. Analysis of Other Neurological Disorders (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,188		
Background RH	372	1.21 (0.85,1.73)	0.281
Low RH	235	1.31 (0.90,1.89)	0.161
High RH	235	1.23 (0.85,1.77)	0.271
Low plus High RH	470	1.27 (0.95,1.69)	0.106

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	285	45 (15.8)	1.13 (1.01,1.26)	0.038
Medium	286	54 (18.9)		
High	284	73 (25.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
842	0.97 (0.84,1.11)	0.625

[a] Relative risk for a twofold increase in 1987 dioxin.

The Model 3 unadjusted analysis displayed significant differences between Ranch Hands in each of the low, high, and low plus high dioxin categories and Comparisons (Table 11-6(e): Est. RR=1.48, p=0.023; Est. RR=1.62, p=0.005; and Est. RR=1.55, p=0.001, respectively). Each result became nonsignificant after adjustment for covariates (Table 11-6(f): p>0.10 for each adjusted result). The Model 3 contrast of Ranch Hands in the background dioxin category with Comparisons was nonsignificant in both the unadjusted and adjusted analysis (Table 11-6(g,h): p>0.28 for the unadjusted and adjusted analyses).

A significant positive association between other neurological disorders and the 1987 dioxin levels was found in the Model 4 unadjusted analysis (Table 11-6(g): Est. RR=1.13, p=0.038). After adjustment for covariates, the association became nonsignificant (Table 11-6(h): p=0.625).

11.2.2.2 Physical Examination Variables – Cranial Nerve Function

11.2.2.2.1 Smell

A marginally significant difference was found between Ranch Hand and Comparison enlisted flyers from the Model 1 unadjusted analysis of an abnormal sense of smell (Table 11-7(a): Est. RR=7.70, p=0.060). After adjustment for covariates, the result was nonsignificant (Table 11-7(b): p=0.148). All other Model 1 contrasts, as well as all other results from Models 2 through 4, were nonsignificant (Table 11-7(a–h): p>0.12 for each remaining analysis).

Table 11-7. Analysis of Smell

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***862***	***20 (2.3)***	***1.54 (0.81,2.89)***	***0.186***
	Comparison	***1,247***	***19 (1.5)***		
Officer	Ranch Hand	337	5 (1.5)	0.73 (0.25,2.14)	0.562
	Comparison	492	10 (2.0)		
Enlisted Flyer	Ranch Hand	151	6 (4.0)	7.70 (0.92,64.65)	0.060
	Comparison	187	1 (0.5)		
Enlisted Groundcrew	Ranch Hand	374	9 (2.4)	1.73 (0.66,4.51)	0.266
	Comparison	568	8 (1.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.20 (0.60,2.36)***	***0.609***
Officer	0.53 (0.16,1.71)	0.286
Enlisted Flyer	5.12 (0.56,46.70)	0.148
Enlisted Groundcrew	1.57 (0.58,4.27)	0.376

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	159	5 (3.1)	0.94 (0.58,1.51)	0.782
Medium	162	2 (1.2)		
High	156	4 (2.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 11-7. Analysis of Smell (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
469	0.83 (0.46,1.50)	0.534

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race because of the sparse number of Ranch Hands with an abnormal sense of smell.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,209	18 (1.5)		
Background RH	378	8 (2.1)	1.42 (0.61,3.31)	0.420
Low RH	238	7 (2.9)	2.01 (0.83,4.86)	0.122
High RH	239	4 (1.7)	1.14 (0.38,3.40)	0.821
Low plus High RH	477	11 (2.3)	1.51 (0.69,3.29)	0.300

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,191		
Background RH	373	1.04 (0.40,2.73)	0.929
Low RH	234	1.57 (0.61,4.06)	0.353
High RH	235	0.82 (0.23,2.92)	0.758
Low plus High RH	469	1.13 (0.48,2.68)	0.777

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-7. Analysis of Smell (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	285	7 (2.5)	0.89 (0.65,1.23)	0.481
Medium	286	6 (2.1)		
High	284	6 (2.1)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
842	0.83 (0.56,1.22)	0.333

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race because of the sparse number of Ranch Hands with an abnormal sense of smell.

11.2.2.2.2 Visual Fields

All results from the analysis of visual fields from Models 1, 3, and 4 were nonsignificant (Table 11-8(a,b,e–h): p>0.38 for each analysis). A significant positive association between visual fields and initial dioxin was found in both the unadjusted and adjusted Model 2 analyses (Table 11-8(c,d): Est. RR=3.93, p=0.040; and Adj. RR=4.37, p=0.049, respectively). One Ranch Hand in the high initial dioxin category had abnormal visual fields.

Table 11-8. Analysis of Visual Fields

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***2 (0.2)***	***0.57 (0.11,2.97)***	***0.493***
	Comparison	***1,245***	***5 (0.4)***		
Officer	Ranch Hand	340	0 (0.0)	--	0.999[a]
	Comparison	492	1 (0.2)		
Enlisted Flyer	Ranch Hand	151	1 (0.7)	0.61 (0.06,6.83)	0.691
	Comparison	186	2 (1.1)		
Enlisted Groundcrew	Ranch Hand	375	1 (0.3)	0.76 (0.07,8.36)	0.819
	Comparison	567	2 (0.4)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with abnormal visual fields.
--: Results not presented because of the sparse number of participants with abnormal visual fields.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.49 (0.09,2.64)***	***0.387***
Officer	--	--
Enlisted Flyer	0.48 (0.04,5.78)	0.566
Enlisted Groundcrew	0.70 (0.06,8.00)	0.778

--: Results not presented because of the sparse number of participants with abnormal visual fields.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	0 (0.0)	3.93 (0.93,16.64)	0.040
Medium	162	0 (0.0)		
High	157	1 (0.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 11-8. Analysis of Visual Fields (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
476	4.37 (0.84,22.64)	0.049

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race, occupation, insecticide exposure, industrial chemicals exposure, degreasing chemicals exposure, and diabetic class because of the sparse number of Ranch Hands with abnormal visual fields.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,207	5 (0.4)		
Background RH	380	1 (0.3)	0.70 (0.08,6.09)	0.746
Low RH	239	0 (0.0)	--	0.694[c]
High RH	240	1 (0.4)	0.92 (0.11,8.03)	0.940
Low plus High RH	479	1 (0.2)	--	0.853[c]

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with abnormal visual fields.
--: Results not presented because of the sparse number of participants with abnormal visual fields.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,189		
Background RH	375	0.86 (0.10,7.83)	0.897
Low RH	235	--	--
High RH	236	0.57 (0.06,5.52)	0.629
Low plus High RH	471	--	--

[a] Relative risk and confidence interval relative to Comparisons.
--: Results not presented because of the sparse number of participants with abnormal visual fields.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-8. Analysis of Visual Fields (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	287	1 (0.4)	1.43 (0.62,3.31)	0.421
Medium	287	0 (0.0)		
High	285	1 (0.4)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
853	1.40 (0.58,3.38)	0.456

[a] Relative risk for a twofold increase in 1987 dioxin

Note: Results are not adjusted for race, occupation, insecticide exposure, degreasing chemicals exposure, and diabetic class because of the sparse number of Ranch Hands with abnormal visual fields.

11.2.2.2.3 Light Reaction

More Comparisons than Ranch Hands had an abnormal light reaction, and the unadjusted and adjusted Model 1 analyses combining all occupations were significant (Table 11-9(a,b): Est. RR=0.12, p=0.007 for the unadjusted analysis; and Adj. RR=0.13, p=0.010 for the adjusted analysis). Results were nonsignificant when examined separately for each occupation in both the unadjusted and adjusted analyses (Table 11-9(a,b): p>0.17 for each remaining Model 1 contrast).

Table 11-9. Analysis of Light Reaction

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***861***	***1 (0.1)***	***0.12 (0.02,0.92)***	***0.007***
	Comparison	***1,247***	***12 (1.0)***		
Officer	Ranch Hand	336	0 (0.0)	--	0.399[a]
	Comparison	493	3 (0.6)		
Enlisted Flyer	Ranch Hand	151	1 (0.7)	0.31 (0.03,2.76)	0.291
	Comparison	187	4 (2.1)		
Enlisted Groundcrew	Ranch Hand	374	0 (0.0)	--	0.173[a]
	Comparison	567	5 (0.9)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormal light reaction.

--: Results not presented because of the sparse number of participants with an abnormal light reaction.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.13 (0.02,0.98)***	***0.010***
Officer	--	--
Enlisted Flyer	0.36 (0.04,3.38)	0.371
Enlisted Groundcrew	--	--

--: Results not presented because of the sparse number of participants with an abnormal light reaction.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)	p-Value
Low	160	0 (0.0)	--	--
Medium	162	0 (0.0)		
High	156	0 (0.0)		

--: Results not presented because of the sparse number of participants with an abnormal light reaction.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)	p-Value
--	--	--

--: Results not presented because of the sparse number of participants with an abnormal light reaction.

Table 11-9. Analysis of Light Reaction (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,209	11 (0.9)		
Background RH	376	1 (0.3)	0.30 (0.04,2.35)	0.252
Low RH	239	0 (0.0)	--	0.283[c]
High RH	239	0 (0.0)	--	0.283[c]
Low plus High RH	478	0 (0.0)	--	0.079[c]

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormal light reaction.
--: Results not presented because of the sparse number of participants with an abnormal light reaction.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,191		
Background RH	371	0.38 (0.05,3.03)	0.359
Low RH	235	--	--
High RH	235	--	--
Low plus High RH	470	--	--

[a] Relative risk and confidence interval relative to Comparisons.
--: Results not presented because of the sparse number of participants with an abnormal light reaction.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	284	0 (0.0)	0.77 (0.18,3.29)	0.715
Medium	286	1 (0.4)		
High	284	0 (0.0)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 11-9. Analysis of Light Reaction (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
848	0.75 (0.18,3.12)	0.681

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race, occupation, insecticide exposure, industrial chemicals exposure, degreasing chemicals exposure, and diabetic class because of the sparse number of participants with an abnormal light reaction.

The Model 2 analysis of light reaction was not possible because of the absence of any Ranch Hands with an abnormal light reaction and an initial dioxin estimate.

The unadjusted Model 3 analysis displayed a marginally significant difference between Ranch Hands in the low plus high dioxin category and Comparisons (Table 11-9(e): p=0.079). The percentage of participants with an abnormal light reaction was 0.0 percent for Ranch Hands in the low plus high category and 0.9 percent for Comparisons. All other Model 3 contrasts examined, as well as the Model 4 analysis results, were nonsignificant (Table 11-9(e–h): p>0.25 for each remaining Model 3 contrast and Model 4 analysis).

11.2.2.2.4 Ocular Movement

All results from the analyses of ocular movement from Models 1 through 4 were nonsignificant (Table 11-10(a–h): p>0.15 for each analysis).

Table 11-10. Analysis of Ocular Movement

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***14 (1.6)***	***1.19 (0.58,2.43)***	***0.632***
	Comparison	***1,249***	***17 (1.4)***		
Officer	Ranch Hand	340	2 (0.6)	0.58 (0.11,2.99)	0.513
	Comparison	493	5 (1.0)		
Enlisted Flyer	Ranch Hand	151	3 (2.0)	1.87 (0.31,11.37)	0.494
	Comparison	187	2 (1.1)		
Enlisted Groundcrew	Ranch Hand	375	9 (2.4)	1.37 (0.55,3.42)	0.493
	Comparison	569	10 (1.8)		

Table 11-10. Analysis of Ocular Movement (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1.17 (0.56,2.42)*	*0.675*
Officer	0.56 (0.11,2.90)	0.485
Enlisted Flyer	1.76 (0.29,10.81)	0.543
Enlisted Groundcrew	1.37 (0.54,3.45)	0.508

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	4 (2.5)	0.77 (0.44,1.32)	0.315
Medium	162	4 (2.5)		
High	157	2 (1.3)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
471	0.74 (0.40,1.36)	0.318

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race and insecticide exposure because of the sparse number of participants with an abnormal ocular movement.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	14 (1.2)		
Background RH	380	4 (1.1)	0.93 (0.30,2.85)	0.896
Low RH	239	5 (2.1)	1.82 (0.65,5.10)	0.256
High RH	240	5 (2.1)	1.79 (0.63,5.04)	0.271
Low plus High RH	479	10 (2.1)	1.80 (0.79,4.10)	0.159

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-10. Analysis of Ocular Movement (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Comparison	1,193		
Background RH	375	1.18 (0.37,3.73)	0.781
Low RH	235	1.76 (0.61,5.07)	0.291
High RH	236	1.32 (0.45,3.83)	0.614
Low plus High RH	471	1.52 (0.65,3.55)	0.328

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**	
1987 Dioxin	**n**	**Number (%) Abnormal**	**Estimated Relative Risk (95% C.I.)[a]**	**p-Value**
Low	287	3 (1.1)	1.09 (0.77,1.54)	0.643
Medium	287	5 (1.7)		
High	285	6 (2.1)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
846	0.91 (0.63,1.32)	0.614

[a] Relative risk for a twofold increase in 1987 dioxin.

11.2.2.2.5 Facial Sensation

All analyses of facial sensation in Models 1 through 4 were nonsignificant (Table 11-11(a–h): p>0.45 for each analysis).

Table 11-11. Analysis of Facial Sensation

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***865***	***2 (0.2)***	***1.44 (0.20,10.27)***	***0.714***
	Comparison	***1,248***	***2 (0.2)***		
Officer	Ranch Hand	339	1 (0.3)	1.46 (0.09,23.35)	0.791
	Comparison	493	1 (0.2)		
Enlisted Flyer	Ranch Hand	151	0 (0.0)	--	0.999[a]
	Comparison	187	1 (0.5)		
Enlisted Groundcrew	Ranch Hand	375	1 (0.3)	--	0.834[a]
	Comparison	568	0 (0.0)		

[a]P-value determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormal facial sensation.
--: Results not presented because of the sparse number of participants with an abnormal facial sensation.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.38 (0.19,9.87)***	***0.750***
Officer	1.45 (0.09,23.48)	0.792
Enlisted Flyer	--	--
Enlisted Groundcrew	--	--

--: Results not presented because of the sparse number of participants with an abnormal facial sensation.

Note: Results are not adjusted for race, insecticide exposure, and diabetic class because of the sparse number of participants with an abnormal facial sensation.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	1 (0.6)	0.45 (0.04,5.19)	0.455
Medium	162	0 (0.0)		
High	157	0 (0.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 11-11. Analysis of Facial Sensation (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
476	0.55 (0.06,5.38)	0.553

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race, occupation, insecticide exposure, industrial chemicals exposure, degreasing chemicals exposure, and diabetic class because of the sparse number of Ranch Hands with an abnormal facial sensation.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,210	2 (0.2)		
Background RH	379	1 (0.3)	1.77 (0.16,19.96)	0.646
Low RH	239	1 (0.4)	2.46 (0.22,27.39)	0.463
High RH	240	0 (0.0)	--	0.999[c]
Low plus High RH	479	1 (0.2)	--	0.999[c]

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormal facial sensation.
--: Results not presented because of the sparse number of participants with an abnormal facial sensation.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-11. Analysis of Facial Sensation (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,209		
Background RH	376	1.70 (0.14,19.96)	0.672
Low RH	238	2.04 (0.18,23.31)	0.564
High RH	238	--	--
Low plus High RH	476	--	--

[a] Relative risk and confidence interval relative to Comparisons.
--: Results not presented because of the sparse number of participants with an abnormal facial sensation.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for race, insecticide exposure, and diabetic class because of the sparse number of participants with an abnormal facial sensation.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	286	1 (0.4)	0.75 (0.27,2.11)	0.572
Medium	287	1 (0.4)		
High	285	0 (0.0)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
852	0.79 (0.23,2.66)	0.694

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race, occupation, insecticide exposure, and diabetic class because of the sparse number of Ranch Hands with an abnormal facial sensation.

11.2.2.2.6 Corneal Reflex

Statistical analysis of corneal reflex was not performed because of the absence of abnormalities among Ranch Hands. A corneal reflex abnormality was noted in one Black enlisted groundcrew Comparison.

11.2.2.2.7 Jaw Clench

Each result obtained from the analyses of jaw clench conducted from Models 1 through 4 was nonsignificant (Table 11-12(a–h): p>0.32 for each analysis).

Table 11-12. Analysis of Jaw Clench

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	**Group**	**n**	**Number (%) Deviated**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***866***	***2 (0.2)***	--	***0.327***[a]
	Comparison	***1,249***	***0 (0.0)***		
Officer	Ranch Hand	340	2 (0.6)	--	0.325[a]
	Comparison	493	0 (0.0)		
Enlisted Flyer	Ranch Hand	151	0 (0.0)	--	--
	Comparison	187	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	375	0 (0.0)	--	--
	Comparison	569	0 (0.0)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a deviated jaw clench.

--: Results not presented because of the sparse number of participants with a deviated jaw clench.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	**Adjusted Relative Risk (95% C.I.)**	**p-Value**
All	--	--
Officer	--	--
Enlisted Flyer	--	--
Enlisted Groundcrew	--	--

--: Results not presented because of the sparse number of participants with a deviated jaw clench.

Table 11-12. Analysis of Jaw Clench (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Deviated	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	0 (0.0)	0.59 (0.09,3.87)	0.539
Medium	162	1 (0.6)		
High	157	0 (0.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
476	0.59 (0.08,4.24)	0.562

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race, occupation, insecticide exposure, industrial chemicals exposure, degreasing chemicals exposure, and diabetic class because of the sparse number of Ranch Hands with a deviated jaw clench.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Deviated	Est. Relative Risk (95% C.I.)	p-Value
Comparison	1,211	0 (0.0)		
Background RH	380	1 (0.3)	--	0.540[a]
Low RH	239	1 (0.4)	--	0.366[a]
High RH	240	0 (0.0)	--	--
Low plus High RH	479	1 (0.2)	--	0.631[a]

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a deviated jaw clench.
--: Results not presented because of the sparse number of participants with a deviated jaw clench.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-12. Analysis of Jaw Clench (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
Comparison	--		
Background RH	--	--	--
Low RH	--	--	--
High RH	--	--	--
Low plus High RH	--	--	--

--: Results not presented because of the sparse number of participants with a deviated jaw clench.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Deviated	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	287	0 (0.0)	0.92 (0.35,2.44)	0.864
Medium	287	2 (0.7)		
High	285	0 (0.0)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
853	1.02 (0.34,3.08)	0.969

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race, occupation, insecticide exposure, and diabetic class because of the sparse number of Ranch Hands with a deviated jaw clench.

11.2.2.2.8 Smile

Each result obtained from the analyses of smile conducted from Models 1 through 4 was nonsignificant (Table 11-13(a–h): p≥0.11 for each analysis).

Table 11-13. Analysis of Smile

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***7 (0.8)***	***2.54 (0.74,8.69)***	***0.129***
	Comparison	***1,249***	***4 (0.3)***		
Officer	Ranch Hand	340	1 (0.3)	0.72 (0.07,8.02)	0.793
	Comparison	493	2 (0.4)		
Enlisted Flyer	Ranch Hand	151	1 (0.7)	--	0.915[a]
	Comparison	187	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	375	5 (1.3)	3.83 (0.74,19.85)	0.110
	Comparison	569	2 (0.4)		

[a]P-value determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormal smile.
--: Results not presented because of the sparse number of participants with an abnormal smile.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***2.45 (0.71,8.50)***	***0.149***
Officer	0.71 (0.06,7.91)	0.777
Enlisted Flyer	--	--
Enlisted Groundcrew	3.62 (0.69,19.00)	0.128

--: Results not presented because of the sparse number of participants with an abnormal smile.

Note: Results are not adjusted for diabetic class because of the sparse number of participants with an abnormal smile.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	1 (0.6)	1.38 (0.70,2.70)	0.372
Medium	162	1 (0.6)		
High	157	2 (1.3)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 11-13. Analysis of Smile (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
476	1.50 (0.75,3.02)	0.274

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race, occupation, industrial chemicals exposure, degreasing chemicals exposure, and diabetic class because of the sparse number of Ranch Hands with an abnormal smile.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	4 (0.3)		
Background RH	380	3 (0.8)	2.61 (0.57,11.87)	0.214
Low RH	239	2 (0.8)	2.49 (0.45,13.68)	0.295
High RH	240	2 (0.8)	2.35 (0.42,13.05)	0.328
Low plus High RH	479	4 (0.8)	2.42 (0.60,9.77)	0.215

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,210		
Background RH	377	3.14 (0.65,15.08)	0.152
Low RH	238	2.38 (0.42,13.43)	0.326
High RH	238	1.80 (0.30,10.67)	0.517
Low plus High RH	476	2.07 (0.50,8.57)	0.315

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for diabetic class because of the sparse number of Ranch Hands with an abnormal smile.

Table 11-13. Analysis of Smile (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	287	2 (0.7)	1.16 (0.72,1.88)	0.541
Medium	287	2 (0.7)		
High	285	3 (1.1)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
853	0.99 (0.59,1.65)	0.972

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for diabetic class because of the sparse number of Ranch Hands with an abnormal smile.

11.2.2.2.9 Palpebral Fissure

All results from the analyses of palpebral fissure from Models 1 through 4 were nonsignificant (Table 11-14(a–h): p>0.32 for each analysis).

Table 11-14. Analysis of Palpebral Fissure

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***7 (0.8)***	***0.84 (0.33,2.14)***	***0.713***
	Comparison	***1,249***	***12 (1.0)***		
Officer	Ranch Hand	340	2 (0.6)	0.58 (0.11,2.99)	0.513
	Comparison	493	5 (1.0)		
Enlisted Flyer	Ranch Hand	151	1 (0.7)	1.24 (0.08,19.99)	0.879
	Comparison	187	1 (0.5)		
Enlisted Groundcrew	Ranch Hand	375	4 (1.1)	1.01 (0.28,3.61)	0.986
	Comparison	569	6 (1.1)		

Table 11-14. Analysis of Palpebral Fissure (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.71 (0.26,1.94)***	***0.502***
Officer	0.63 (0.12,3.31)	0.582
Enlisted Flyer	0.87 (0.05,14.32)	0.921
Enlisted Groundcrew	0.90 (0.25,3.27)	0.876

Note: Results are not adjusted for diabetic class because of the sparse number of participants with an abnormal palpebral fissure. Results for analyses stratified by occupation also are not adjusted for lifetime alcohol history because of the sparse number of participants with an abnormal palpebral fissure.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	2 (1.3)	1.15 (0.50,2.64)	0.750
Medium	162	0 (0.0)		
High	157	1 (0.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
476	1.25 (0.54,2.93)	0.613

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race, occupation, insecticide exposure, degreasing chemicals exposure, and diabetic class because of the sparse number of Ranch Hands with an abnormal palpebral fissure.

Table 11-14. Analysis of Palpebral Fissure (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	12 (1.0)		
Background RH	380	4 (1.1)	1.20 (0.38,3.78)	0.759
Low RH	239	2 (0.8)	0.81 (0.18,3.66)	0.785
High RH	240	1 (0.4)	0.37 (0.05,2.91)	0.347
Low plus High RH	479	3 (0.6)	0.55 (0.14,2.10)	0.381

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,210		
Background RH	377	0.96 (0.26,3.60)	0.955
Low RH	238	0.79 (0.17,3.64)	0.761
High RH	238	0.35 (0.04,2.84)	0.324
Low plus High RH	476	0.52 (0.13,2.05)	0.352

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for diabetic class because of the sparse number of participants with an abnormal palpebral fissure.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	287	2 (0.7)	1.05 (0.64,1.73)	0.840
Medium	287	4 (1.4)		
High	285	1 (0.4)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 11-14. Analysis of Palpebral Fissure (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
853	1.17 (0.65,2.12)	0.598

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race, occupation, insecticide exposure, and diabetic class because of the sparse number of participants with an abnormal palpebral fissure.

11.2.2.2.10 Balance

All results from the analyses of balance from Models 1 through 4 were nonsignificant (Table 11-15(a–h): p>0.12 for each analysis).

Table 11-15. Analysis of Balance

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***7 (0.8)***	***1.44 (0.50,4.13)***	***0.494***
	Comparison	***1,248***	***7 (0.6)***		
Officer	Ranch Hand	340	5 (1.5)	3.66 (0.71,19.00)	0.122
	Comparison	493	2 (0.4)		
Enlisted Flyer	Ranch Hand	151	0 (0.0)	--	0.999[a]
	Comparison	186	1 (0.5)		
Enlisted Groundcrew	Ranch Hand	375	2 (0.5)	0.76 (0.14,4.16)	0.749
	Comparison	569	4 (0.7)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with abnormal balance.

--: Results not presented because of the sparse number of participants with abnormal balance.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.38 (0.47,4.03)***	***0.553***
Officer	3.37 (0.64,17.73)	0.151
Enlisted Flyer	--	--
Enlisted Groundcrew	0.73 (0.13,4.07)	0.719

--: Results not presented because of the sparse number of participants with abnormal balance.

Table 11-15. Analysis of Balance (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	0 (0.0)	1.27 (0.48,3.35)	0.638
Medium	162	1 (0.6)		
High	157	1 (0.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
476	1.65 (0.61,4.45)	0.350

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race, occupation, insecticide exposure, and diabetic class because of the sparse number of Ranch Hands with abnormal balance.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,210	7 (0.6)		
Background RH	380	5 (1.3)	2.52 (0.78,8.10)	0.121
Low RH	239	1 (0.4)	0.70 (0.09,5.74)	0.741
High RH	240	1 (0.4)	0.66 (0.08,5.43)	0.699
Low plus High RH	479	2 (0.4)	0.68 (0.14,3.31)	0.633

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-15. Analysis of Balance (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,192		
Background RH	375	2.54 (0.74,8.72)	0.138
Low RH	235	0.63 (0.08,5.24)	0.667
High RH	236	0.63 (0.07,5.49)	0.672
Low plus High RH	471	0.63 (0.13,3.11)	0.567

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	287	3 (1.1)	0.88 (0.52,1.50)	0.642
Medium	287	2 (0.7)		
High	285	2 (0.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
846	0.95 (0.52,1.73)	0.860

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race and occupation because of the sparse number of participants with abnormal balance.

11.2.2.2.11 Gag Reflex

Because of the absence of gag reflex abnormalities among Ranch Hands, statistical analysis was not performed. One gag reflex abnormality was present for a non-Black enlisted flyer Comparison.

11.2.2.2.12 Speech

The Model 2 adjusted analysis of speech revealed a marginally significant inverse association between initial dioxin and speech (Table 11-16(d): Adj. RR=0.19, p=0.078). All other analysis results from Models 1 through 4 were nonsignificant (Table 11-16(a–c,e–h): p>0.14 for each remaining analysis).

Table 11-16. Analysis of Speech

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***4 (0.5)***	***0.57 (0.18,1.84)***	***0.334***
	Comparison	***1,249***	***10 (0.8)***		
Officer	Ranch Hand	340	1 (0.3)	0.72 (0.07,8.02)	0.793
	Comparison	493	2 (0.4)		
Enlisted Flyer	Ranch Hand	151	0 (0.0)	--	0.999[a]
	Comparison	187	1 (0.5)		
Enlisted Groundcrew	Ranch Hand	375	3 (0.8)	0.65 (0.17,2.52)	0.531
	Comparison	569	7 (1.2)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with abnormal speech.

--: Results not presented because of the sparse number of participants with abnormal speech.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.60 (0.18,1.97)***	***0.388***
Officer	0.76 (0.07,8.59)	0.828
Enlisted Flyer	--	--
Enlisted Groundcrew	0.66 (0.16,2.63)	0.551

--: Results not presented because of the sparse number of participants with abnormal speech.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	2 (1.3)	0.29 (0.03,2.42)	0.143
Medium	162	0 (0.0)		
High	157	0 (0.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 11-16. Analysis of Speech (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
476	0.19 (0.02,2.32)	0.078

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for occupation and diabetic class because of the sparse number of Ranch Hands with abnormal speech.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	9 (0.7)		
Background RH	380	2 (0.5)	0.81 (0.17,3.83)	0.793
Low RH	239	2 (0.8)	1.07 (0.23,5.02)	0.929
High RH	240	0 (0.0)	--	0.374[c]
Low plus High RH	479	2 (0.4)	--	0.678[c]

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with abnormal speech.
--: Results not presented because of the sparse number of participants with abnormal speech.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,193		
Background RH	375	1.09 (0.22,5.46)	0.919
Low RH	235	1.38 (0.28,6.71)	0.688
High RH	236	--	--
Low plus High RH	471	--	--

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-16. Analysis of Speech (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	287	2 (0.7)	0.77 (0.37,1.59)	0.462
Medium	287	2 (0.7)		
High	285	0 (0.0)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
853	0.73 (0.36,1.47)	0.370

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for occupation and diabetic class because of the sparse number of Ranch Hands with abnormal speech.

11.2.2.2.13 Tongue Position Relative to Midline

Each result obtained from the Model 1 through 4 analyses of tongue position relative to midline was nonsignificant (Table 11-17(a–h): p>0.32 for each analysis).

Table 11-17. Analysis of Tongue Position Relative to Midline

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Deviated	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***2 (0.2)***	***--***	***0.327***[a]
	Comparison	***1,249***	***0 (0.0)***		
Officer	Ranch Hand	340	2 (0.6)	--	0.325[a]
	Comparison	493	0 (0.0)		
Enlisted Flyer	Ranch Hand	151	0 (0.0)	--	--
	Comparison	187	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	375	0 (0.0)	--	--
	Comparison	569	0 (0.0)		

[a]P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a deviated tongue position relative to midline.
--: Results not presented because of the sparse number of participants with a deviated tongue position relative to midline.

Table 11-17. Analysis of Tongue Position Relative to Midline (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	--	--
Officer	--	--
Enlisted Flyer	--	--
Enlisted Groundcrew	--	--

--: Results not presented because of the sparse number of participants with a deviated tongue position relative to midline.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Deviated	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	0 (0.0)	0.59 (0.09,3.87)	0.539
Medium	162	1 (0.6)		
High	157	0 (0.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
476	0.59 (0.08,4.24)	0.562

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race, occupation, insecticide exposure, industrial chemicals exposure, degreasing chemicals exposure, and diabetic class because of the sparse number of Ranch Hands with a deviated tongue position relative to midline.

Table 11-17. Analysis of Tongue Position Relative to Midline (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Deviated	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	0 (0.0)		
Background RH	380	1 (0.3)	--	0.540[c]
Low RH	239	1 (0.4)	--	0.366[c]
High RH	240	0 (0.0)	--	--
Low plus High RH	479	1 (0.2)	--	0.631[c]

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a deviated tongue position relative to midline.
--: Results not presented because of the sparse number of participants with a deviated tongue position relative to midline.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
Comparison	--		
Background RH	--	--	--
Low RH	--	--	--
High RH	--	--	--
Low plus High RH	--	--	--

--: Results not presented because of the sparse number of participants with a deviated tongue position relative to midline.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Deviated	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	287	0 (0.0)	0.92 (0.35,2.44)	0.864
Medium	287	2 (0.7)		
High	285	0 (0.0)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 11-17. Analysis of Tongue Position Relative to Midline (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
853	1.02 (0.34,3.08)	0.969

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race, occupation, insecticide exposure, and diabetic class because of the sparse number of Ranch Hands with a deviated tongue position relative to midline.

11.2.2.2.14 Palate and Uvula Movement

Each result obtained from the Model 1 through 4 analyses of the palate and uvula movement was nonsignificant (Table 11-18(a–h): p>0.36 for each analysis).

Table 11-18. Analysis of Palate and Uvula Movement

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Deviated	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***1 (0.1)***	**--**	***0.854***[a]
	Comparison	***1,249***	***0 (0.0)***		
Officer	Ranch Hand	340	1 (0.3)	--	0.852[a]
	Comparison	493	0 (0.0)		
Enlisted Flyer	Ranch Hand	151	0 (0.0)	--	--
	Comparison	187	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	375	0 (0.0)	--	--
	Comparison	569	0 (0.0)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a deviated palate and uvula movement.
--: Results not presented because of the sparse number of participants with a deviated palate and uvula movement.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	**--**	**--**
Officer	--	--
Enlisted Flyer	--	--
Enlisted Groundcrew	--	--

--: Results not presented because of the sparse number of participants with a deviated palate and uvula movement.

Table 11-18. Analysis of Palate and Uvula Movement (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Deviated	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	0 (0.0)	0.59 (0.09,3.87)	0.539
Medium	162	1 (0.6)		
High	157	0 (0.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
476	0.59 (0.08,4.24)	0.562

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race, occupation, insecticide exposure, industrial chemicals exposure, degreasing chemicals exposure, and diabetic class because of the sparse number of Ranch Hands with a deviated palate and uvula movement.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Deviated	Est. Relative Risk (95% C.I.)	p-Value
Comparison	1,211	0 (0.0)		
Background RH	380	0 (0.0)	--	--
Low RH	239	1 (0.4)	--	0.366[a]
High RH	240	0 (0.0)	--	--
Low plus High RH	479	1 (0.2)	--	0.631[a]

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a deviated palate and uvula movement.
--: Results not presented because of the sparse number of participants with a deviated palate and uvula movement.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-18. Analysis of Palate and Uvula Movement (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
Comparison	--		
Background RH	--	--	--
Low RH	--	--	--
High RH	--	--	--
Low plus High RH	--	--	--

--: Results not presented because of the sparse number of participants with a deviated palate and uvula movement.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Deviated	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	287	0 (0.0)	1.13 (0.31,4.05)	0.857
Medium	287	1 (0.4)		
High	285	0 (0.0)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
853	1.19 (0.32,4.46)	0.800

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race, occupation, insecticide exposure, industrial chemicals exposure, degreasing chemicals exposure, and diabetic class because of the sparse number of Ranch Hands with a deviated palate and uvula movement.

11.2.2.2.15 Cranial Nerve Index

All results from the analyses of cranial nerve index from Models 1 through 4 were nonsignificant (Table 11-19(a–h): p≥0.11 for each analysis).

Table 11-19. Analysis of Cranial Nerve Index

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***850***	***56 (6.6)***	***1.15 (0.80,1.65)***	***0.452***
	Comparison	***1,245***	***72 (5.8)***		
Officer	Ranch Hand	329	17 (5.2)	0.98 (0.52,1.83)	0.941
	Comparison	492	26 (5.3)		
Enlisted Flyer	Ranch Hand	151	13 (8.6)	1.66 (0.71,3.89)	0.246
	Comparison	186	10 (5.4)		
Enlisted Groundcrew	Ranch Hand	370	26 (7.0)	1.11 (0.66,1.88)	0.683
	Comparison	567	36 (6.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.01 (0.69,1.48)***	***0.940***
Officer	0.88 (0.46,1.68)	0.694
Enlisted Flyer	1.23 (0.49,3.08)	0.656
Enlisted Groundcrew	1.05 (0.61,1.80)	0.856

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	157	13 (8.3)	0.86 (0.63,1.17)	0.331
Medium	162	9 (5.6)		
High	153	8 (5.2)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
464	0.75 (0.53,1.08)	0.110

[a] Relative risk for a twofold increase in initial dioxin.

Table 11-19. Analysis of Cranial Nerve Index (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,207	68 (5.6)		
Background RH	371	25 (6.7)	1.27 (0.79,2.05)	0.329
Low RH	236	19 (8.1)	1.45 (0.86,2.47)	0.166
High RH	236	11 (4.7)	0.78 (0.41,1.51)	0.469
Low plus High RH	472	30 (6.4)	1.07 (0.68,1.69)	0.776

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,189		
Background RH	366	1.20 (0.72,2.02)	0.484
Low RH	232	1.29 (0.74,2.24)	0.369
High RH	232	0.60 (0.30,1.22)	0.158
Low plus High RH	464	0.88 (0.54,1.43)	0.604

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	280	18 (6.4)	0.93 (0.77,1.13)	0.462
Medium	282	21 (7.5)		
High	281	16 (5.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 11-19. Analysis of Cranial Nerve Index (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
830	0.88 (0.71,1.10)	0.254

[a] Relative risk for a twofold increase in 1987 dioxin.

11.2.2.3 Physical Examination Variables – Musculoskeletal and Vertebral Column Function

11.2.2.3.1 Neck Range of Motion

From the Model 1 unadjusted and adjusted analyses of neck range of motion, differences between Ranch Hands and Comparisons were significant across all occupations and within enlisted flyers (Table 11-20(a,b): Est. RR=1.33, p=0.016, Adj. RR=1.35, p=0.015, respectively, for all occupations combined; Est. RR=2.03, p=0.009; Adj. RR=1.97, p=0.016, respectively, for enlisted flyers). Both contrasts showed more Ranch Hands than Comparisons with a restricted neck range of motion. All other Model 1 contrasts were nonsignificant (Table 11-20(a,b): p>0.12 for each remaining contrast).

Table 11-20. Analysis of Neck Range of Motion

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***165 (19.1)***	***1.33 (1.06,1.67)***	***0.016***
	Comparison	***1,249***	***188 (15.1)***		
Officer	Ranch Hand	340	70 (20.6)	1.32 (0.92,1.88)	0.126
	Comparison	493	81 (16.4)		
Enlisted Flyer	Ranch Hand	151	41 (27.2)	2.03 (1.19,3.46)	0.009
	Comparison	187	29 (15.5)		
Enlisted Groundcrew	Ranch Hand	375	54 (14.4)	1.06 (0.73,1.54)	0.764
	Comparison	569	78 (13.7)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.35 (1.06,1.72)***	***0.015***
Officer	1.31 (0.90,1.89)	0.153
Enlisted Flyer	1.97 (1.13,3.42)	0.016
Enlisted Groundcrew	1.16 (0.78,1.71)	0.466

Table 11-20. Analysis of Neck Range of Motion (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	38 (23.8)	0.85 (0.72,1.02)	0.069
Medium	162	39 (24.1)		
High	157	26 (16.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
471	0.91 (0.74,1.13)	0.411

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	180 (14.9)		
Background RH	380	60 (15.8)	1.16 (0.84,1.60)	0.366
Low RH	239	56 (23.4)	1.73 (1.23,2.43)	0.002
High RH	240	47 (19.6)	1.31 (0.91,1.87)	0.142
Low plus High RH	479	103 (21.5)	1.50 (1.15,1.97)	0.003

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-20. Analysis of Neck Range of Motion (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,193		
Background RH	375	1.12 (0.80,1.57)	0.523
Low RH	235	1.60 (1.12,2.29)	0.010
High RH	236	1.55 (1.05,2.29)	0.028
Low plus High RH	471	1.57 (1.18,2.11)	0.002

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	287	48 (16.7)	1.03 (0.92,1.15)	0.632
Medium	287	60 (20.9)		
High	285	55 (19.3)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
846	1.09 (0.94,1.26)	0.267

[a] Relative risk for a twofold increase in 1987 dioxin.

The unadjusted Model 2 analysis displayed a marginally significant inverse association between neck range of motion and initial dioxin (Table 11-20(c): Est. RR=0.85, p=0.069). After adjustment for covariates, the association was nonsignificant (Table 11-20(d): p=0.411).

Both the unadjusted and adjusted Model 3 analyses of neck range of motion displayed a significant difference between Ranch Hands in the low dioxin category and Comparisons (Table 11-20(e,f): Est. RR=1.73, p=0.002 and Adj. RR=1.60, p=0.010) and between Ranch Hands in the low plus high dioxin category and Comparisons (Table 11-20(e,f): Est. RR=1.50, p=0.003 and Adj. RR=1.57, p=0.002). In addition, the adjusted contrast between Ranch Hands in the high category and Comparisons was significant (Table 11-20(f): Adj. RR=1.55, p=0.028). All significant contrasts showed more Ranch

Hands than Comparisons with neck range of motion abnormalities. Other Model 3 contrasts, as well as the Model 4 analyses of neck range of motion, were nonsignificant (Table 11-20(e–h): p>0.14 for each remaining analysis).

11.2.2.4 Physical Examination Variables – Peripheral Nerve Status

11.2.2.4.1 Pinprick

A marginally significant difference between Ranch Hands in the high dioxin category and Comparisons was found in the Model 3 unadjusted analysis of pinprick, showing more Ranch Hands than Comparisons with a pinprick abnormality (Table 11-21(e): Est. RR=1.64, p=0.062). After adjustment for covariates, the difference was nonsignificant (Table 11-21(f): p=0.126). All other analysis results from Models 1 through 4 for pinprick were nonsignificant (Table 11-21(a–h): p≥0.11 for each remaining analysis).

Table 11-21. Analysis of Pinprick

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***822***	***57 (6.9)***	***1.24 (0.86,1.79)***	***0.244***
	Comparison	***1,185***	***67 (5.7)***		
Officer	Ranch Hand	322	20 (6.2)	1.35 (0.72,2.51)	0.350
	Comparison	469	22 (4.7)		
Enlisted Flyer	Ranch Hand	145	19 (13.1)	1.81 (0.87,3.75)	0.110
	Comparison	182	14 (7.7)		
Enlisted Groundcrew	Ranch Hand	355	18 (5.1)	0.87 (0.48,1.57)	0.638
	Comparison	534	31 (5.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.19 (0.81,1.76)***	***0.368***
Officer	1.28 (0.67,2.43)	0.451
Enlisted Flyer	1.81 (0.84,3.89)	0.131
Enlisted Groundcrew	0.85 (0.45,1.60)	0.618

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	152	11 (7.2)	1.10 (0.86,1.41)	0.460
Medium	151	13 (8.6)		
High	150	12 (8.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 11-21. Analysis of Pinprick (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
445	1.29 (0.92,1.81)	0.134

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,149	63 (5.5)		
Background RH	362	19 (5.3)	1.03 (0.61,1.76)	0.900
Low RH	226	15 (6.6)	1.20 (0.67,2.15)	0.542
High RH	227	21 (9.3)	1.64 (0.98,2.76)	0.062
Low plus High RH	453	36 (8.0)	1.40 (0.91,2.16)	0.123

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,132		
Background RH	357	1.11 (0.63,1.95)	0.716
Low RH	222	0.95 (0.51,1.77)	0.868
High RH	223	1.55 (0.88,2.73)	0.126
Low plus High RH	445	1.21 (0.77,1.93)	0.410

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-21. Analysis of Pinprick (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	272	15 (5.5)	1.15 (0.96,1.37)	0.137
Medium	275	16 (5.8)		
High	268	24 (9.0)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
Analysis Results for Log_2 (1987 Dioxin + 1)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
802	1.12 (0.88,1.42)	0.345

[a] Relative risk for a twofold increase in 1987 dioxin.

11.2.2.4.2 Light Touch

All results from the analyses of light touch from Models 1 through 4 were nonsignificant (Table 11-22(a–h): p>0.16 for each analysis).

Table 11-22. Analysis of Light Touch

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***822***	***38 (4.6)***	***1.23 (0.79,1.91)***	***0.363***
	Comparison	***1,185***	***45 (3.8)***		
Officer	Ranch Hand	322	15 (4.7)	1.71 (0.80,3.65)	0.163
	Comparison	469	13 (2.8)		
Enlisted Flyer	Ranch Hand	145	12 (8.3)	1.55 (0.65,3.70)	0.322
	Comparison	182	10 (5.5)		
Enlisted Groundcrew	Ranch Hand	355	11 (3.1)	0.74 (0.36,1.55)	0.432
	Comparison	534	22 (4.1)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.13 (0.71,1.81)***	***0.597***
Officer	1.67 (0.77,3.61)	0.193
Enlisted Flyer	1.40 (0.56,3.50)	0.470
Enlisted Groundcrew	0.67 (0.31,1.47)	0.321

Table 11-22. Analysis of Light Touch (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	152	9 (5.9)	0.92 (0.66,1.28)	0.616
Medium	151	7 (4.6)		
High	150	7 (4.7)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
445	1.01 (0.65,1.59)	0.956

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,149	43 (3.7)		
Background RH	362	13 (3.6)	1.01 (0.54,1.92)	0.965
Low RH	226	12 (5.3)	1.42 (0.74,2.74)	0.295
High RH	227	11 (4.9)	1.25 (0.63,2.46)	0.528
Low plus High RH	453	23 (5.1)	1.33 (0.79,2.24)	0.283

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-22. Analysis of Light Touch (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,132		
Background RH	357	1.07 (0.54,2.10)	0.852
Low RH	222	1.12 (0.55,2.27)	0.751
High RH	223	1.09 (0.53,2.26)	0.808
Low plus High RH	445	1.11 (0.64,1.93)	0.718

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	272	11 (4.0)	1.02 (0.81,1.28)	0.865
Medium	275	12 (4.4)		
High	268	13 (4.9)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
802	1.01 (0.75,1.36)	0.940

[a] Relative risk for a twofold increase in 1987 dioxin.

11.2.2.4.3 Muscle Status

Both the unadjusted and adjusted Model 1 analyses of muscle status displayed a marginally significant difference between Ranch Hands and Comparisons (Table 11-23(a,b): Est. RR=1.54, p=0.064 and Adj. RR=1.50, p=0.094). The contrast of Ranch Hand and Comparison enlisted groundcrew revealed a marginally significant result in the unadjusted analysis and a significant result in the adjusted analysis (Table 11-23(a,b): Est. RR=2.06, p=0.062 and Adj. RR=2.24, p=0.046). Both contrasts showed more Ranch Hands than Comparisons with a muscle status abnormality. All other Model 1 contrasts, as well as the Model 2 analysis of muscle status, were nonsignificant (Table 11-23(a–d): p>0.23 for each remaining Model 1 contrast and each Model 2 analysis).

Table 11-23. Analysis of Muscle Status

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***39 (4.5)***	***1.54 (0.98,2.44)***	***0.064***
	Comparison	***1,248***	***37 (3.0)***		
Officer	Ranch Hand	340	13 (3.8)	1.05 (0.51,2.17)	0.897
	Comparison	493	18 (3.7)		
Enlisted Flyer	Ranch Hand	151	10 (6.6)	1.82 (0.68,4.91)	0.235
	Comparison	187	7 (3.7)		
Enlisted Groundcrew	Ranch Hand	375	16 (4.3)	2.06 (0.97,4.42)	0.062
	Comparison	568	12 (2.1)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.50 (0.93,2.40)***	***0.094***
Officer	0.98 (0.47,2.05)	0.960
Enlisted Flyer	1.72 (0.63,4.70)	0.289
Enlisted Groundcrew	2.24 (1.01,4.93)	0.046

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	10 (6.3)	0.87 (0.62,1.23)	0.418
Medium	162	9 (5.6)		
High	157	5 (3.2)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
471	0.95 (0.64,1.41)	0.792

[a] Relative risk for a twofold increase in initial dioxin.

Table 11-23. Analysis of Muscle Status (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,210	35 (2.9)		
Background RH	380	14 (3.7)	1.23 (0.65,2.31)	0.530
Low RH	239	14 (5.9)	2.11 (1.12,3.99)	0.021
High RH	240	10 (4.2)	1.52 (0.74,3.12)	0.254
Low plus High RH	479	24 (5.0)	1.79 (1.05,3.06)	0.033

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,192		
Background RH	375	1.22 (0.63,2.35)	0.550
Low RH	235	1.90 (0.98,3.66)	0.056
High RH	236	1.58 (0.73,3.39)	0.242
Low plus High RH	471	1.73 (0.99,3.04)	0.056

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	287	10 (3.5)	1.02 (0.82,1.27)	0.863
Medium	287	15 (5.2)		
High	285	13 (4.6)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 11-23. Analysis of Muscle Status (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
846	0.98 (0.76,1.27)	0.897

[a] Relative risk for a twofold increase in 1987 dioxin.

The Model 3 unadjusted analysis revealed significantly more Ranch Hands in the low dioxin category with an abnormal muscle status than Comparisons (Table 11-23(e): Est. RR=2.11, p=0.021). Significantly more Ranch Hands in the low plus high dioxin category than Comparisons also had an abnormal muscle status (Table 11-23(e): Est. RR=1.79, p=0.033). Both contrasts were marginally significant in the adjusted analysis (Table 11-23(f): Adj. RR=1.90, p=0.056 for the low dioxin category contrast; and Adj. RR=1.73, p=0.056 for the low plus high dioxin category contrast). All other Model 3 contrasts, as well as the Model 4 analysis results, were nonsignificant (Table 11-23(e–h): p>0.24 for each remaining analysis).

11.2.2.4.4 Patellar Reflex

The Model 1 analysis of the patellar reflex revealed a marginally significant difference between Ranch Hands and Comparison enlisted flyers in both the unadjusted and adjusted analyses (Table 11-24(a,b): Est. RR=0.17, p=0.100 and Adj. RR=0.16, p=0.089). The prevalence of a patellar reflex abnormality was higher among Comparisons than Ranch Hands. All other Model 1 contrasts were nonsignificant (Table 11-24(a,b): p>0.40 for each remaining Model 1 contrast).

Table 11-24. Analysis of Patellar Reflex

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***865***	***24 (2.8)***	***0.99 (0.58,1.67)***	***0.962***
	Comparison	***1,246***	***35 (2.8)***		
Officer	Ranch Hand	340	12 (3.5)	1.09 (0.51,2.34)	0.823
	Comparison	493	16 (3.3)		
Enlisted Flyer	Ranch Hand	151	1 (0.7)	0.17 (0.02,1.40)	0.100
	Comparison	186	7 (3.8)		
Enlisted Groundcrew	Ranch Hand	374	11 (2.9)	1.40 (0.61,3.21)	0.425
	Comparison	567	12 (2.1)		

Table 11-24. Analysis of Patellar Reflex (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.97 (0.56,1.67)***	***0.910***
Officer	1.05 (0.48,2.29)	0.901
Enlisted Flyer	0.16 (0.02,1.32)	0.089
Enlisted Groundcrew	1.43 (0.61,3.34)	0.408

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	159	5 (3.1)	1.18 (0.82,1.71)	0.374
Medium	162	3 (1.9)		
High	157	7 (4.5)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
470	1.81 (1.10,2.99)	0.019

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,209	33 (2.7)		
Background RH	380	9 (2.4)	0.91 (0.43,1.93)	0.812
Low RH	238	7 (2.9)	1.06 (0.46,2.44)	0.882
High RH	240	8 (3.3)	1.17 (0.53,2.58)	0.693
Low plus High RH	478	15 (3.1)	1.12 (0.60,2.08)	0.727

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-24. Analysis of Patellar Reflex (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,191		
Background RH	375	0.88 (0.40,1.91)	0.742
Low RH	234	0.86 (0.37,2.02)	0.737
High RH	236	1.39 (0.60,3.26)	0.446
Low plus High RH	470	1.10 (0.57,2.10)	0.778

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	287	8 (2.8)	1.08 (0.83,1.42)	0.568
Medium	286	7 (2.5)		
High	285	9 (3.2)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
845	1.15 (0.80,1.64)	0.447

[a] Relative risk for a twofold increase in 1987 dioxin.

The unadjusted Model 2 analysis of patellar reflex was nonsignificant (Table 11-24(c): p=0.374). After adjustment for covariates, a significant positive association between patellar reflex and initial dioxin was revealed (Table 11-24(d): Adj. RR=1.81, p=0.019). As initial dioxin increased in Ranch Hands, the prevalence of an abnormal patellar reflex increased.

All results from the analyses of patellar reflex from Models 3 and 4 were nonsignificant (Table 11-24(e–h): p>0.44 for each Model 3 and 4 analysis).

11.2.2.4.5 Achilles Reflex

The Model 2 adjusted analysis revealed a marginally significant association between an abnormal Achilles reflex and initial dioxin (Table 11-25 (d): Adj. RR=1.22, p=0.075). The marginally significant result indicates that Achilles reflex abnormalities increased in Ranch Hands as the initial dioxin levels increased. All other analysis results for Achilles reflex from Models 1 through 4 were nonsignificant (Table 11-25(a–h): p>0.15 for each analysis).

Table 11-25. Analysis of Achilles Reflex

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***865***	***153 (17.7)***	***1.10 (0.88,1.39)***	***0.410***
	Comparison	***1,244***	***203 (16.3)***		
Officer	Ranch Hand	340	67 (19.7)	1.22 (0.86,1.75)	0.267
	Comparison	491	82 (16.7)		
Enlisted Flyer	Ranch Hand	151	30 (19.9)	1.00 (0.58,1.71)	0.995
	Comparison	186	37 (19.9)		
Enlisted Groundcrew	Ranch Hand	374	56 (15.0)	1.01 (0.70,1.46)	0.947
	Comparison	567	84 (14.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.07 (0.84,1.37)***	***0.594***
Officer	1.17 (0.80,1.70)	0.413
Enlisted Flyer	0.91 (0.51,1.60)	0.737
Enlisted Groundcrew	1.05 (0.71,1.55)	0.815

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	29 (18.1)	1.04 (0.87,1.23)	0.688
Medium	162	31 (19.1)		
High	157	33 (21.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 11-25. Analysis of Achilles Reflex (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
471	1.22 (0.98,1.51)	0.075

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,206	197 (16.3)		
Background RH	379	57 (15.0)	0.99 (0.72,1.37)	0.963
Low RH	239	46 (19.3)	1.20 (0.84,1.71)	0.325
High RH	240	47 (19.6)	1.16 (0.81,1.65)	0.425
Low plus High RH	479	93 (19.4)	1.18 (0.89,1.55)	0.247

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,188		
Background RH	374	0.96 (0.68,1.35)	0.811
Low RH	235	0.97 (0.66,1.42)	0.880
High RH	236	1.32 (0.89,1.95)	0.168
Low plus High RH	471	1.13 (0.84,1.52)	0.416

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-25. Analysis of Achilles Reflex (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	286	44 (15.4)	1.07 (0.95,1.21)	0.250
Medium	287	49 (17.1)		
High	285	57 (20.0)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
845	1.12 (0.96,1.31)	0.157

[a] Relative risk for a twofold increase in 1987 dioxin.

11.2.2.4.6 Biceps Reflex

A significant increase of Ranch Hands in the low dioxin category relative to Comparisons was found from the unadjusted Model 3 analysis of the biceps reflex (Table 11-26(e): Est. RR=2.88, p=0.029). The result was marginally significant in the adjusted analysis (Table 11-26(f): Adj. RR=2.52, p=0.064). All other Model 3 contrasts, as well as all other analysis results from Models 1, 2, and 4, were nonsignificant (Table 11-26(a–h): p≥0.12 for all remaining analyses).

Table 11-26. Analysis of Biceps Reflex

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***12 (1.4)***	***1.45 (0.65,3.24)***	***0.369***
	Comparison	***1,248***	***12 (1.0)***		
Officer	Ranch Hand	340	5 (1.5)	1.21 (0.37,4.00)	0.753
	Comparison	493	6 (1.2)		
Enlisted Flyer	Ranch Hand	151	2 (1.3)	1.24 (0.17,8.92)	0.830
	Comparison	187	2 (1.1)		
Enlisted Groundcrew	Ranch Hand	375	5 (1.3)	1.91 (0.51,7.14)	0.339
	Comparison	568	4 (0.7)		

Table 11-26. Analysis of Biceps Reflex (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.31 (0.57,3.05)***	***0.527***
Officer	1.13 (0.33,3.80)	0.848
Enlisted Flyer	1.34 (0.18,9.89)	0.776
Enlisted Groundcrew	1.61 (0.39,6.58)	0.509

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	3 (1.9)	0.72 (0.41,1.24)	0.203
Medium	162	6 (3.7)		
High	157	1 (0.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
471	0.87 (0.44,1.70)	0.675

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,210	12 (1.0)		
Background RH	380	2 (0.5)	0.61 (0.14,2.77)	0.524
Low RH	239	7 (2.9)	2.88 (1.12,7.44)	0.029
High RH	240	3 (1.3)	1.10 (0.30,3.96)	0.887
Low plus High RH	479	10 (2.1)	1.78 (0.73,4.35)	0.209

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-26. Analysis of Biceps Reflex (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,192		
Background RH	375	0.27 (0.03,2.13)	0.213
Low RH	235	2.52 (0.95,6.70)	0.064
High RH	236	1.37 (0.35,5.29)	0.651
Low plus High RH	471	1.85 (0.73,4.69)	0.193

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	287	0 (0.0)	1.16 (0.80,1.68)	0.437
Medium	287	8 (2.8)		
High	285	4 (1.4)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
846	1.52 (0.89,2.61)	0.120

[a] Relative risk for a twofold increase in 1987 dioxin.

11.2.2.4.7 Babinski Reflex

All analysis results from Models 1 through 3 for Babinski reflex were nonsignificant (Table 11-27(a–f): p>0.23 for each analysis). The result from the unadjusted Model 4 analysis of Babinski reflex was marginally significant and inverse in direction (Table 11-27(g): Est. RR=0.58, p=0.056). After adjustment for covariates, the association between Babinski reflex and the 1987 dioxin levels was nonsignificant (Table 11-27(h): p=0.223).

Table 11-27. Analysis of Babinski Reflex

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***8 (0.9)***	***0.88 (0.36,2.14)***	***0.785***
	Comparison	***1,246***	***13 (1.0)***		
Officer	Ranch Hand	340	3 (0.9)	2.18 (0.36,13.12)	0.394
	Comparison	492	2 (0.4)		
Enlisted Flyer	Ranch Hand	151	1 (0.7)	0.40 (0.04,3.93)	0.435
	Comparison	185	3 (1.6)		
Enlisted Groundcrew	Ranch Hand	375	4 (1.1)	0.76 (0.23,2.53)	0.650
	Comparison	569	8 (1.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.81 (0.31,2.10)***	***0.666***
Officer	2.16 (0.35,13.17)	0.403
Enlisted Flyer	0.36 (0.04,3.59)	0.385
Enlisted Groundcrew	0.64 (0.16,2.51)	0.526

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	1 (0.6)	0.89 (0.28,2.86)	0.848
Medium	162	0 (0.0)		
High	157	1 (0.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
476	1.08 (0.34,3.42)	0.896

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race, occupation, insecticide exposure, industrial chemicals exposure, and diabetic class because of the sparse number of Ranch Hands with an abnormal Babinski reflex.

Table 11-27. Analysis of Babinski Reflex (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,208	11 (0.9)		
Background RH	380	5 (1.3)	1.48 (0.50,4.33)	0.477
Low RH	239	1 (0.4)	0.46 (0.06,3.55)	0.452
High RH	240	1 (0.4)	0.45 (0.06,3.50)	0.444
Low plus High RH	479	2 (0.4)	0.45 (0.10,2.05)	0.303

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,190		
Background RH	375	1.53 (0.45,5.14)	0.496
Low RH	235	0.38 (0.05,3.05)	0.364
High RH	236	0.41 (0.05,3.33)	0.405
Low plus High RH	471	0.40 (0.08,1.85)	0.239

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	287	5 (1.7)	0.58 (0.32,1.03)	0.056
Medium	287	1 (0.4)		
High	285	1 (0.4)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 11-27. Analysis of Babinski Reflex (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
853	0.65 (0.33,1.29)	0.223

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for diabetic class because of the sparse number of Ranch Hands with an abnormal Babinski reflex.

11.2.2.4.8 Polyneuropathy Severity Index

The results from the Model 1 unadjusted analysis of the polyneuropathy severity index revealed a significant difference between Ranch Hands and Comparisons in the percentage of participants with a moderate polyneuropathy severity index (Table 11-28(a): Est. RR=2.37, p=0.015). A marginally significant difference between Ranch Hand and Comparison enlisted flyers in the percentage of participants with a moderate polyneuropathy severity index also was observed (Table 11-28(a): Est. RR=4.54, p=0.062). Results were consistent in the adjusted analysis for both contrasts (Table 11-28(b): Adj. RR=2.32, p=0.020 for all occupations combined; Adj.RR=4.13, p=0.083 for enlisted flyers). All other Model 1 contrasts performed were nonsignificant (Table 11-28(a,b): p>0.11 for each remaining Model 1 contrast).

The Model 2 adjusted analysis revealed a significant positive association between a moderate polyneuropathy severity index and initial dioxin (Table 11-28(d): Adj. RR=1.52, p=0.042). All other Model 2 results were nonsignificant (Table 11-28(c,d): p>0.16 for the remaining Model 2 analyses results).

The Model 3 unadjusted analysis of the polyneuropathy severity index displayed several significant associations between categorized dioxin and a moderate polyneuropathy severity index. The contrasts of Ranch Hands in the low, high, and low plus high dioxin categories versus Comparisons each were significant and displayed more Ranch Hands than Comparisons with a moderate polyneuropathy severity index (Table 11-28(e): Est. RR=2.76, p=0.032; Est. RR=2.64, p=0.042; and Est. RR=2.70, p=0.011, respectively). The results remained significant in the adjusted analysis for the contrast of Comparisons with Ranch Hands in the high and the low plus high dioxin categories, and was marginally significant for the contrast of Ranch Hands in the low dioxin category with Comparisons (Table 11-28(f): Adj. RR=3.06, p=0.024; Adj. RR=2.68, p=0.014; and Adj. RR=2.35, p=0.079, respectively). The background Ranch Hand contrast was nonsignificant in both the unadjusted and adjusted analyses (Table 10-28(e): p>0.61 for each contrast).

Table 11-28. Analysis of Polyneuropathy Severity Index

(a) MODEL 1: RANCH HANDS VS. COMPARISONS - UNADJUSTED									
			Number (%)			Moderate vs. None/Mild		Severe vs. None/Mild	
Occupational Category	Group	n	None/Mild	Moderate	Severe	Est. Relative Risk (95% C.I.)	p-Value	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***821***	***796 (97.0)***	***21 (2.6)***	***4 (0.5)***	***2.37 (1.18,4.76)***	***0.015***	***5.87 (0.65,52.61)***	***0.114***
	Comparison	***1,182***	***1,168 (98.8)***	***13 (1.1)***	***1 (0.1)***				
Officer	Ranch Hand	322	312 (96.9)	7 (2.2)	3 (0.9)	1.73 (0.58,5.19)	0.330	--	0.130
	Comparison	468	462 (98.7)	6 (1.3)	0 (0.0)				
Enlisted Flyer	Ranch Hand	145	138 (95.2)	7 (4.8)	0 (0.0)	4.54 (0.93,22.20)	0.062	--	--
	Comparison	181	179 (98.9)	2 (1.1)	0 (0.0)				
Enlisted Groundcrew	Ranch Hand	354	346 (97.7)	7 (2.0)	1 (0.3)	2.13 (0.67,6.77)	0.199	1.52 (0.09,24.45)	0.766
	Comparison	533	527 (98.9)	5 (0.9)	1 (0.2)				

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a severe polyneuropathy severity index.

--: Results not presented because of the sparse number of participants with a severe polyneuropathy severity index.

Table 11-28. Analysis of Polyneuropathy Severity Index (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED				
	Moderate vs. None/Mild		Severe vs. None/Mild	
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Adj. Relative Risk (95% C.I.)	p-Value
All	***2.32 (1.14,4.73)***	***0.020***	***5.44 (0.59,50.52)***	***0.136***
Officer	1.72 (0.57,5.24)	0.338	--	--
Enlisted Flyer	4.13 (0.83,20.52)	0.083	--	--
Enlisted Groundcrew	2.16 (0.67,7.01)	0.200	1.64 (0.09,29.24)	0.738

--: Results not presented because of the sparse number of participants with a severe polyneuropathy severity index.

Note: Results are not adjusted for diabetic class because of the sparse number of participants with a moderate or severe polyneuropathy severity index. Results for all occupations combined also are not adjusted for occupation because of the sparse number of participants with a moderate or severe polyneuropathy severity index.

Table 11-28. Analysis of Polyneuropathy Severity Index (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED								
	Initial Dioxin Category Summary Statistics				Analysis Results for Log$_2$ (Initial Dioxin)[a]			
		Number (%)			Moderate vs. None/Mild		Severe vs. None/Mild	
Initial Dioxin Category	n	None/Mild	Moderate	Severe	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
Low	152	146 (96.1)	4 (2.6)	2 (1.3)	1.29 (0.90,1.87)	0.168	0.68 (0.23,1.98)	0.476
Medium	151	147 (97.4)	4 (2.7)	0 (0.0)				
High	150	143 (95.3)	6 (4.0)	1 (0.7)				

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED				
	Analysis Results for Log$_2$ (Initial Dioxin)			
	Moderate vs. None/Mild		Severe vs. None/Mild	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
450	1.52 (1.02,2.28)	0.042	0.87 (0.24,3.20)	0.832

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for occupation and diabetic class because of the sparse number of Ranch Hands with a moderate or severe polyneuropathy severity index.

Table 11-28. Analysis of Polyneuropathy Severity Index (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED								
		Number (%)			Moderate vs. None/Mild		Severe vs. None/Mild	
Dioxin Category	n	None/Mild	Moderate	Severe	Est. Relative Risk (95% C.I.)[ab]	p-Value	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,146	1,132 (98.8)	13 (1.1)	1 (0.1)				
Background RH	361	355 (98.3)	5 (1.4)	1 (0.3)	1.30 (0.46,3.71)	0.619	3.03 (0.19,49.25)	0.435
Low RH	226	217 (96.0)	7 (3.1)	2 (0.9)	2.76 (1.09,7.02)	0.032	10.54 (0.95,116.83)	0.055
High RH	227	219 (96.5)	7 (3.1)	1 (0.4)	2.64 (1.03,6.73)	0.042	5.41 (0.33,87.73)	0.235
Low plus High RH	453	436 (96.3)	14 (3.1)	3 (0.7)	2.70 (1.26,5.81)	0.011	7.54 (0.75,75.71)	0.086

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-28. Analysis of Polyneuropathy Severity Index (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED					
		Moderate vs. None/Mild		Severe vs. None/Mild	
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,145				
Background RH	358	1.29 (0.45,3.70)	0.641	2.59 (0.15,43.89)	0.511
Low RH	225	2.35 (0.90,6.09)	0.079	7.43 (0.62,89.56)	0.114
High RH	225	3.06 (1.16,8.11)	0.024	9.83 (0.52,186.07)	0.128
Low plus High RH	450	2.68 (1.22,5.90)	0.014	8.55 (0.77,94.34)	0.080

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for occupation and diabetic class because of the sparse number of participants with a moderate or severe polyneuropathy severity index.

Table 11-28. Analysis of Polyneuropathy Severity Index (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category	1987 Dioxin Category Summary Statistics				Analysis Results for Log_2 (1987 Dioxin + 1)			
		Number (%)			Moderate vs. None/Mild		Severe vs. None/Mild	
	n	None/Mild	Moderate	Severe	Est. Relative Risk (95% C.I.)[a]	p-Value	Est. Relative Risk (95% C.I.)[a]	p-Value
Low	271	267 (98.5)	4 (1.5)	0 (0.0)	1.38 (1.04,1.84)	0.024	1.13 (0.59,2.15)	0.717
Medium	275	266 (96.7)	6 (2.2)	3 (1.1)				
High	268	258 (96.3)	9 (3.4)	1 (0.4)				

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin + 1)			
	Moderate vs. None/Mild		Severe vs. None/Mild	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
808	1.51 (1.09,2.09)	0.013	1.48 (0.62,3.50)	0.376

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for occupation and diabetic class because of the sparse number of Ranch Hands with a moderate or severe polyneuropathy severity index.

The Model 3 unadjusted analysis of participants with a severe polyneuropathy severity index showed a marginally significant difference between Ranch Hands in the low dioxin category and Comparisons, and between Ranch Hands in the low plus high dioxin category and Comparisons (Table 11-28(e): Est. RR=10.54, p=0.055 and Est. RR=7.54, p=0.086, respectively). The contrast of Ranch Hands in the low plus high dioxin category remained marginally significant in the adjusted analysis (Table 11-28(f): Adj. RR=8.55, p=0.080). All other Model 3 contrasts of participants with a severe polyneuropathy severity index were nonsignificant (Table 11-28(e,f): p>0.11 for each remaining contrast).

The results from the Model 4 analysis of the polyneuropathy severity index were significant in both the unadjusted and adjusted analyses, showing a positive association between the percentage of Ranch Hands with a moderate polyneuropathy severity index and 1987 dioxin (Table 11-28(g,h): Est. RR=1.38, p=0.024 for the unadjusted analysis; and Adj. RR=1.51, p=0.013 for the adjusted analysis). The association between 1987 dioxin and a severe polyneuropathy severity index was nonsignificant (Table 11-28(g,h): p>0.37 for both the unadjusted and adjusted analyses).

11.2.2.4.9 Polyneuropathy Prevalence Index

All analysis results contrasting Ranch Hands and Comparisons on the polyneuropathy prevalence index in Models 1 and 3 were nonsignificant (Table 11-29(a,b,e,f): p>0.20 for each Model 1 and 3 contrast).

Table 11-29. Analysis of Polyneuropathy Prevalence Index

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***821***	***130 (15.8)***	***1.06 (0.83,1.35)***	***0.668***
	Comparison	***1,183***	***179 (15.1)***		
Officer	Ranch Hand	322	55 (17.1)	1.08 (0.74,1.58)	0.694
	Comparison	468	75 (16.0)		
Enlisted Flyer	Ranch Hand	145	29 (20.0)	0.92 (0.53,1.57)	0.752
	Comparison	182	39 (21.4)		
Enlisted Groundcrew	Ranch Hand	354	46 (13.0)	1.08 (0.72,1.61)	0.725
	Comparison	533	65 (12.2)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.99 (0.76,1.28)***	***0.923***
Officer	1.02 (0.68,1.51)	0.941
Enlisted Flyer	0.86 (0.48,1.52)	0.601
Enlisted Groundcrew	1.03 (0.67,1.59)	0.877

Table 11-29. Analysis of Polyneuropathy Prevalence Index (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	152	23 (15.1)	1.09 (0.91,1.31)	0.344
Medium	151	28 (18.5)		
High	150	29 (19.3)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
445	1.30 (1.03,1.65)	0.029

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,147	175 (15.3)		
Background RH	361	47 (13.0)	0.89 (0.63,1.27)	0.530
Low RH	226	38 (16.8)	1.10 (0.75,1.62)	0.618
High RH	227	42 (18.5)	1.18 (0.81,1.72)	0.376
Low plus High RH	453	80 (17.7)	1.14 (0.85,1.53)	0.370

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-29. Analysis of Polyneuropathy Prevalence Index (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,130		
Background RH	356	0.83 (0.57,1.20)	0.315
Low RH	222	0.86 (0.57,1.30)	0.484
High RH	223	1.31 (0.86,1.98)	0.206
Low plus High RH	445	1.06 (0.77,1.46)	0.708

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	271	39 (14.4)	1.09 (0.96,1.24)	0.198
Medium	275	38 (13.8)		
High	268	50 (18.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
801	1.16 (0.98,1.37)	0.080

[a] Relative risk for a twofold increase in 1987 dioxin.

The Model 2 unadjusted analysis of the polyneuropathy prevalence index was nonsignificant (Table 11-29(c): p=0.344). After adjustment for covariates, the association between the polyneuropathy prevalence index and initial dioxin was positive and significant (Table 11-29(d): Adj. RR=1.30, p=0.029). Similarly, the Model 4 unadjusted analysis was nonsignificant (Table 11-29(g): p=0.198, but the association between the polyneuropathy prevalence index and 1987 dioxin was marginally significant in the adjusted analysis (Table 11-29(h): Adj. RR=1.16, p=0.080).

11.2.2.4.10 Multiple Polyneuropathy Index

The difference in the multiple polyneuropathy index between Ranch Hands and Comparisons was significant and showed more Ranch Hands than Comparisons with an abnormal multiple polyneuropathy

index (Table 11-30(a): Est. RR=1.58, p=0.046). After adjustment for covariates, the difference became marginally significant (Table 11-30(b): Adj. RR=1.51, p=0.092). All other Model 1 contrasts were nonsignificant (Table 11-30(a,b): p>0.15 for all remaining Model 1 contrasts).

Table 11-30. Analysis of Multiple Polyneuropathy Index

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	**Group**	**n**	**Number (%) Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***821***	***41 (5.0)***	***1.58 (1.01,2.49)***	***0.046***
	Comparison	***1,183***	***38 (3.2)***		
Officer	Ranch Hand	322	16 (5.0)	1.39 (0.69,2.79)	0.358
	Comparison	468	17 (3.6)		
Enlisted Flyer	Ranch Hand	145	13 (9.0)	1.89 (0.79,4.56)	0.155
	Comparison	182	9 (5.0)		
Enlisted Groundcrew	Ranch Hand	354	12 (3.4)	1.52 (0.68,3.43)	0.309
	Comparison	533	12 (2.3)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	**Adjusted Relative Risk (95% C.I.)**	**p-Value**
All	***1.51 (0.94,2.45)***	***0.092***
Officer	1.44 (0.69,2.98)	0.330
Enlisted Flyer	1.77 (0.69,4.56)	0.234
Enlisted Groundcrew	1.43 (0.60,3.39)	0.421

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Number (%) Abnormal**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	152	6 (4.0)	1.30 (0.98,1.73)	0.076
Medium	151	8 (5.3)		
High	150	11 (7.3)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 11-30. Analysis of Multiple Polyneuropathy Index (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
445	1.85 (1.20,2.87)	0.004

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,147	36 (3.1)		
Background RH	361	14 (3.9)	1.29 (0.68,2.43)	0.432
Low RH	226	10 (4.4)	1.42 (0.69,2.90)	0.340
High RH	227	15 (6.6)	2.12 (1.14,3.95)	0.018
Low plus High RH	453	25 (5.5)	1.73 (1.02,2.94)	0.042

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,130		
Background RH	356	1.37 (0.69,2.72)	0.366
Low RH	222	0.96 (0.44,2.10)	0.914
High RH	223	2.38 (1.18,4.82)	0.016
Low plus High RH	445	1.51 (0.84,2.71)	0.165

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-30. Analysis of Multiple Polyneuropathy Index (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	271	11 (4.1)	1.19 (0.96,1.46)	0.110
Medium	275	10 (3.6)		
High	268	18 (6.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
Analysis Results for Log_2 (1987 Dioxin + 1)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
801	1.29 (0.95,1.76)	0.101

[a] Relative risk for a twofold increase in 1987 dioxin.

The Model 2 unadjusted analysis displayed a marginally significant positive association between the multiple polyneuropathy index and initial dioxin (Table 11-30(c): Est. RR=1.30, p=0.076). After adjustment for covariates, the association became significant (Table 11-30(d): Adj. RR=1.85, p=0.004).

A significant difference between Ranch Hands in the high dioxin category and Comparisons was found from the Model 3 unadjusted and adjusted analyses of the multiple polyneuropathy index (Table 11-30(e,f): Est. RR=2.12, p=0.018 and Adj. RR=2.38, p=0.016, respectively). The difference was also significant for the unadjusted contrast of Ranch Hands in the low plus high dioxin category with Comparisons (Table 11-30(e): Est. RR=1.73, p=0.042). This contrast was nonsignificant in the adjusted analysis (Table 11-30(f): p=0.165). The other Model 3 contrasts were nonsignificant in both the unadjusted and adjusted analyses as were the results from the analyses of Model 4 (Table 11-30(e–h): p>0.10 for each remaining Model 3 contrast and Model 4 analyses).

11.2.2.4.11 Confirmed Polyneuropathy Indicator

Differences between Ranch Hands and Comparisons were marginally significant for several contrasts from the Model 1 unadjusted analysis of the confirmed polyneuropathy indicator. For all contrasts, Ranch Hands showed a higher percentage of participants with an abnormal confirmed polyneuropathy indicator than did Comparisons. The difference was marginally significant when examined across all occupations (Table 11-31(a): Est. RR=2.30, p=0.082), for enlisted flyers (Table 11-31(a): p=0.079), and for enlisted groundcrew (Table 11-31(a): Est. RR=7.62, p=0.064). After adjustment for covariates, the results were marginally significant for the analysis across all occupations and for enlisted groundcrew (Table 11-31(b): Adj. RR=2.35, p=0.082; and Adj. RR=8.59, p=0.054, respectively). The analysis of the confirmed polyneuropathy indicator was nonsignificant for officers for both the unadjusted and adjusted analyses (Table 11-31(a,b): p=0.381 and p=0.414, respectively).

Table 11-31. Analysis of Confirmed Polyneuropathy Indicator

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***811***	***11 (1.4)***	***2.30 (0.89,5.95)***	***0.082***
	Comparison	***1,176***	***7 (0.6)***		
Officer	Ranch Hand	318	2 (0.6)	0.49 (0.10,2.43)	0.381
	Comparison	468	6 (1.3)		
Enlisted Flyer	Ranch Hand	142	4 (2.8)	--	0.079[a]
	Comparison	180	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	351	5 (1.4)	7.62 (0.89,65.47)	0.064
	Comparison	528	1 (0.2)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormal confirmed polyneuropathy indicator.
--: Results not presented because of the sparse number of participants with an abnormal confirmed polyneuropathy indicator.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***2.35 (0.88,6.22)***	***0.082***
Officer	0.51 (0.10,2.59)	0.414
Enlisted Flyer	--	--
Enlisted Groundcrew	8.59 (0.97,76.27)	0.054

--: Results not presented because of the sparse number of participants with an abnormal confirmed polyneuropathy indicator.

Note: Results are not adjusted for diabetic class because of the sparse number of participants with an abnormal confirmed polyneuropathy indicator.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	150	2 (1.3)	1.63 (1.05,2.53)	0.033
Medium	150	2 (1.3)		
High	147	5 (3.4)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 11-31. Analysis of Confirmed Polyneuropathy Indicator (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
444	1.98 (1.19,3.29)	0.008

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for occupation, industrial chemicals exposure, degreasing chemicals exposure, and diabetic class because of the sparse number of Ranch Hands with an abnormal confirmed polyneuropathy indicator.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,141	7 (0.6)		
Background RH	358	2 (0.6)	1.06 (0.22,5.16)	0.944
Low RH	224	3 (1.3)	2.08 (0.53,8.17)	0.293
High RH	223	6 (2.7)	3.89 (1.28,11.86)	0.017
Low plus High RH	447	9 (2.0)	2.85 (1.02,7.97)	0.047

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,138		
Background RH	355	0.99 (0.20,4.97)	0.988
Low RH	223	1.56 (0.38,6.40)	0.536
High RH	221	6.04 (1.63,22.42)	0.007
Low plus High RH	444	3.06 (1.02,9.23)	0.047

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for diabetic class because of the sparse number of participants with an abnormal confirmed polyneuropathy indicator.

Table 11-31. Analysis of Confirmed Polyneuropathy Indicator (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	270	1 (0.4)	1.80 (1.26,2.58)	0.002
Medium	271	3 (1.1)		
High	264	7 (2.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
799	2.21 (1.24,3.96)	0.003

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for diabetic class because of the sparse number of Ranch Hands with an abnormal confirmed polyneuropathy indicator.

Both the unadjusted and adjusted analyses from Model 2 displayed a significant positive association between the confirmed polyneuropathy indicator and initial dioxin (Table 11-31(c,d): Est. RR=1.63, p=0.033, and Adj. RR=1.98, p=0.008).

In the unadjusted Model 3 analysis, significant results were found for the contrast of Ranch Hands in the high dioxin category and Ranch Hands in the low plus high dioxin category with Comparisons. The prevalence of an abnormal confirmed polyneuropathy indicator for Ranch Hands in the high dioxin category was significantly greater than for Comparisons (Table 11-31(e,f): Est. RR=3.89, p=0.017 and Adj. RR=6.04, p=0.007). The contrast of Ranch Hands from the low plus high dioxin category with Comparisons also was significant in both unadjusted and adjusted analyses (Table 11-31(e,f): Est. RR=2.85, p=0.047 and Adj. RR=3.06, p=0.047). All other Model 3 contrasts were nonsignificant (Table 11-31(e,f): p>0.29 for each remaining Model 3 contrast).

Both the unadjusted and adjusted analyses of Model 4 displayed a significant positive association between the confirmed polyneuropathy indicator and the 1987 dioxin levels (Table 11-31(g,h): Est. RR=1.80, p=0.002 and Adj. RR=2.21, p=0.003). As 1987 dioxin increased, the prevalence of an abnormal confirmed polyneuropathy indicator increased.

11.2.2.5 Physical Examination Variables – CNS Coordination Processes

11.2.2.5.1 Tremor

All results from the analyses of tremor from Models 1 through 4 were nonsignificant (Table 11-32(a–h): p>0.19 for each analysis).

Table 11-32. Analysis of Tremor

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***60 (6.9)***	***0.95 (0.68,1.33)***	***0.753***
	Comparison	***1,249***	***91 (7.3)***		
Officer	Ranch Hand	340	22 (6.5)	1.11 (0.62,1.96)	0.728
	Comparison	493	29 (5.9)		
Enlisted Flyer	Ranch Hand	151	15 (9.9)	1.26 (0.60,2.68)	0.540
	Comparison	187	15 (8.0)		
Enlisted Groundcrew	Ranch Hand	375	23 (6.1)	0.73 (0.43,1.22)	0.224
	Comparison	569	47 (8.3)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.90 (0.64,1.28)***	***0.564***
Officer	1.06 (0.59,1.89)	0.850
Enlisted Flyer	1.14 (0.53,2.44)	0.734
Enlisted Groundcrew	0.72 (0.42,1.21)	0.212

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	11 (6.9)	1.02 (0.77,1.36)	0.869
Medium	162	10 (6.2)		
High	157	9 (5.7)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
471	1.02 (0.73,1.44)	0.893

[a] Relative risk for a twofold increase in initial dioxin.

Table 11-32. Analysis of Tremor (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	90 (7.4)		
Background RH	380	30 (7.9)	1.05 (0.68,1.62)	0.821
Low RH	239	14 (5.9)	0.78 (0.43,1.39)	0.396
High RH	240	16 (6.7)	0.90 (0.52,1.57)	0.713
Low plus High RH	479	30 (6.3)	0.84 (0.55,1.29)	0.417

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,193		
Background RH	375	1.11 (0.71,1.74)	0.659
Low RH	235	0.71 (0.39,1.28)	0.248
High RH	236	0.79 (0.44,1.40)	0.420
Low plus High RH	471	0.75 (0.48,1.16)	0.194

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	287	23 (8.0)	0.94 (0.79,1.13)	0.527
Medium	287	21 (7.3)		
High	285	16 (5.6)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 11-32. Analysis of Tremor (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
846	0.93 (0.75,1.14)	0.478

[a] Relative risk for a twofold increase in 1987 dioxin.

11.2.2.5.2 Coordination

All results from the analyses of coordination from Models 1 through 4 were nonsignificant (Table 11-33(a–h): p>0.11 for each analysis).

Table 11-33. Analysis of Coordination

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***19 (2.2)***	***0.88 (0.49,1.57)***	***0.663***
	Comparison	***1,247***	***31 (2.5)***		
Officer	Ranch Hand	340	10 (2.9)	1.84 (0.72,4.70)	0.205
	Comparison	493	8 (1.6)		
Enlisted Flyer	Ranch Hand	151	1 (0.7)	0.30 (0.03,2.74)	0.288
	Comparison	186	4 (2.2)		
Enlisted Groundcrew	Ranch Hand	375	8 (2.1)	0.63 (0.27,1.45)	0.279
	Comparison	568	19 (3.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.86 (0.48,1.56)***	***0.622***
Officer	1.65 (0.64,4.26)	0.302
Enlisted Flyer	0.28 (0.03,2.58)	0.263
Enlisted Groundcrew	0.64 (0.27,1.50)	0.305

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	2 (1.3)	0.90 (0.49,1.65)	0.735
Medium	162	4 (2.5)		
High	157	1 (0.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 11-33. Analysis of Coordination (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
n	Analysis Results for Log_2 (Initial Dioxin) Adjusted Relative Risk (95% C.I.)[a]	p-Value
471	1.18 (0.62,2.24)	0.632

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for occupation because of the sparse number of participants with abnormal coordination.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,209	30 (2.5)		
Background RH	380	12 (3.2)	1.33 (0.67,2.65)	0.412
Low RH	239	4 (1.7)	0.66 (0.23,1.90)	0.443
High RH	240	3 (1.3)	0.48 (0.15,1.59)	0.231
Low plus High RH	479	7 (1.5)	0.56 (0.24,1.30)	0.181

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,191		
Background RH	375	1.46 (0.71,3.01)	0.298
Low RH	235	0.61 (0.21,1.79)	0.371
High RH	236	0.42 (0.12,1.42)	0.161
Low plus High RH	471	0.51 (0.22,1.19)	0.117

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-33. Analysis of Coordination (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			**Analysis Results for Log₂ (1987 Dioxin + 1)**	
1987 Dioxin	**n**	**Number (%) Abnormal**	**Estimated Relative Risk (95% C.I.)[a]**	**p-Value**
Low	287	8 (2.8)	0.81 (0.58,1.13)	0.211
Medium	287	7 (2.4)		
High	285	4 (1.4)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log₂ (1987 Dioxin + 1)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
846	0.83 (0.57,1.21)	0.330

[a] Relative risk for a twofold increase in 1987 dioxin.

11.2.2.5.3 Romberg Sign

All results from the analyses of Romberg sign from Models 1 through 4 were nonsignificant (Table 11-34(a–h): p>0.12 for each analysis).

Table 11-34. Analysis of Romberg Sign

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	**Group**	**n**	**Number (%) Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***866***	***7 (0.8)***	***1.44 (0.50,4.13)***	***0.494***
	Comparison	***1,248***	***7 (0.6)***		
Officer	Ranch Hand	340	5 (1.5)	3.66 (0.71,19.00)	0.122
	Comparison	493	2 (0.4)		
Enlisted Flyer	Ranch Hand	151	0 (0.0)	--	0.999[a]
	Comparison	186	1 (0.5)		
Enlisted Groundcrew	Ranch Hand	375	2 (0.5)	0.76 (0.14,4.16)	0.749
	Comparison	569	4 (0.7)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormal Romberg sign.

--: Results not presented because of the sparse number of participants with an abnormal Romberg sign.

Table 11-34. Analysis of Romberg Sign (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.38 (0.47,4.03)***	***0.553***
Officer	3.37 (0.64,17.73)	0.151
Enlisted Flyer	--	--
Enlisted Groundcrew	0.73 (0.13,4.07)	0.719

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	0 (0.0)	1.27 (0.48,3.35)	0.638
Medium	162	1 (0.6)		
High	157	1 (0.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
476	1.65 (0.61,4.45)	0.350

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race, occupation, insecticide exposure, and diabetic class because of the sparse number of participants with an abnormal Romberg sign.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,210	7 (0.6)		
Background RH	380	5 (1.3)	2.52 (0.78,8.10)	0.121
Low RH	239	1 (0.4)	0.70 (0.09,5.74)	0.741
High RH	240	1 (0.4)	0.66 (0.08,5.43)	0.699
Low plus High RH	479	2 (0.4)	0.68 (0.14,3.31)	0.633

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-34. Analysis of Romberg Sign (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,192		
Background RH	375	2.54 (0.74,8.72)	0.138
Low RH	235	0.63 (0.08,5.24)	0.667
High RH	236	0.63 (0.07,5.49)	0.672
Low plus High RH	471	0.63 (0.13,3.11)	0.567

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	287	3 (1.1)	0.88 (0.52,1.50)	0.642
Medium	287	2 (0.7)		
High	285	2 (0.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
846	0.95 (0.52,1.73)	0.860

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race and occupation because of the sparse number of participants with an abnormal Romberg sign.

11.2.2.5.4 Gait

The adjusted Model 1 analysis of gait displayed a marginally significant increase in the prevalence of an abnormal gait for Ranch Hand enlisted groundcrew relative to Comparison enlisted groundcrew (Table 11-35(b): Adj. RR=1.79, p=0.090). All other results from the analysis of gait for Models 1 through 4 were nonsignificant (Table 11-35(a–h): p>0.11 for all remaining analyses).

Table 11-35. Analysis of Gait

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***50 (5.8)***	***1.28 (0.87,1.89)***	***0.214***
	Comparison	***1,249***	***57 (4.6)***		
Officer	Ranch Hand	340	19 (5.6)	1.06 (0.58,1.95)	0.844
	Comparison	493	26 (5.3)		
Enlisted Flyer	Ranch Hand	151	11 (7.3)	1.26 (0.53,2.98)	0.604
	Comparison	187	11 (5.9)		
Enlisted Groundcrew	Ranch Hand	375	20 (5.3)	1.55 (0.82,2.92)	0.178
	Comparison	569	20 (3.5)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.26 (0.83,1.89)***	***0.275***
Officer	1.01 (0.54,1.89)	0.972
Enlisted Flyer	1.05 (0.43,2.59)	0.911
Enlisted Groundcrew	1.79 (0.91,3.49)	0.090

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	8 (5.0)	1.00 (0.74,1.35)	0.998
Medium	162	11 (6.8)		
High	157	7 (4.5)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
471	1.12 (0.79,1.60)	0.530

[a] Relative risk for a twofold increase in initial dioxin.

Table 11-35. Analysis of Gait (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	55 (4.5)		
Background RH	380	23 (6.1)	1.50 (0.91,2.49)	0.115
Low RH	239	11 (4.6)	0.98 (0.51,1.91)	0.963
High RH	240	15 (6.3)	1.28 (0.71,2.32)	0.414
Low plus High RH	479	26 (5.4)	1.12 (0.69,1.83)	0.640

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,193		
Background RH	375	1.52 (0.90,2.59)	0.121
Low RH	235	0.77 (0.38,1.57)	0.479
High RH	236	1.44 (0.76,2.74)	0.262
Low plus High RH	471	1.06 (0.63,1.78)	0.832

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	287	17 (5.9)	1.00 (0.83,1.22)	0.966
Medium	287	15 (5.2)		
High	285	17 (6.0)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 11-35. Analysis of Gait (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
846	0.99 (0.78,1.25)	0.905

[a] Relative risk for a twofold increase in 1987 dioxin.

11.2.2.5.5 CNS Index

All results from the analyses of the CNS index from Models 1 through 4 were nonsignificant (Table 11-36(a–h): p>0.10 for each analysis).

Table 11-36. Analysis of CNS Index

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***107 (12.4)***	***1.05 (0.80,1.37)***	***0.731***
	Comparison	***1,248***	***148 (11.9)***		
Officer	Ranch Hand	340	39 (11.5)	1.08 (0.69,1.67)	0.745
	Comparison	493	53 (10.8)		
Enlisted Flyer	Ranch Hand	151	24 (15.9)	1.07 (0.59,1.94)	0.816
	Comparison	187	28 (15.0)		
Enlisted Groundcrew	Ranch Hand	375	44 (11.7)	0.99 (0.66,1.49)	0.977
	Comparison	568	67 (11.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.99 (0.75,1.31)***	***0.957***
Officer	1.01 (0.64,1.58)	0.975
Enlisted Flyer	0.92 (0.50,1.70)	0.799
Enlisted Groundcrew	1.01 (0.67,1.54)	0.950

Table 11-36. Analysis of CNS Index (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	18 (11.3)	1.00 (0.81,1.24)	0.976
Medium	162	21 (13.0)		
High	157	15 (9.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
471	1.03 (0.80,1.33)	0.840

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,210	146 (12.1)		
Background RH	380	52 (13.7)	1.18 (0.84,1.66)	0.339
Low RH	239	24 (10.0)	0.81 (0.51,1.28)	0.363
High RH	240	30 (12.5)	1.02 (0.67,1.56)	0.923
Low plus High RH	479	54 (11.3)	0.91 (0.65,1.27)	0.576

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-36. Analysis of CNS Index (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,192		
Background RH	375	1.24 (0.86,1.77)	0.249
Low RH	235	0.67 (0.42,1.09)	0.105
High RH	236	0.94 (0.60,1.47)	0.789
Low plus High RH	471	0.80 (0.56,1.13)	0.205

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	287	39 (13.6)	0.97 (0.84,1.12)	0.672
Medium	287	35 (12.2)		
High	285	32 (11.2)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
846	0.94 (0.80,1.10)	0.443

[a] Relative risk for a twofold increase in 1987 dioxin.

11.2.3 Longitudinal Analysis

Longitudinal analyses were conducted on two indices—the cranial nerve function index and the CNS index—to examine whether changes across time differed with respect to group membership (Model 1), initial dioxin (Model 2), and categorized dioxin (Model 3). Model 4 was not examined in longitudinal analyses because 1987 dioxin, the measure of exposure in these models, changes over time and is not available for all participants for 1985 or 1997. For both indices, the longitudinal analyses investigated the differences between the 1985 follow-up examination and the 1997 follow-up examination, because Scripps Clinic conducted both of the neurological examinations. A different clinic performed the

neurological examinations for the 1982 baseline study, and the prevalence of abnormalities was much higher for the neurological parameters in 1982, suggesting a different method of examination.

The longitudinal analyses for all of these variables investigated the difference between the 1985 examination and the 1997 examination. These analyses were used to investigate the temporal effects of dioxin during the 12-year period between 1985 and 1997. Participants considered abnormal in 1985 were not included in the analyses because they were already abnormal before this period. Consequently, only participants considered normal at the 1985 examination (i.e., a normal index) were considered to be at risk when the effects of dioxin over this period of time were explored. The rate of abnormalities under this restriction approximates an incidence rate between 1985 and 1997. That is, an incidence rate is a measure of the rate at which people without a condition develop the condition during a specified period of time (44). Summary statistics are provided for reference purposes for the 1987 and 1992 examinations. All three models were adjusted for age; Models 2 and 3 also were adjusted for the percentage of body fat at the time of the blood measurement of dioxin.

11.2.3.1 Physical Examination Variables

11.2.3.1.1 Cranial Nerve Index

The longitudinal analysis of the cranial nerve index was based on participants with a normal index in 1985. All results from the Model 1 analysis indicate no significant difference between Ranch Hands and Comparisons (Table 11-37(a): p>0.61 for each contrast).

Table 11-37. Longitudinal Analysis of Cranial Nerve Index

(a) MODEL 1: RANCH HANDS VS. COMPARISONS					
		Number (%) Abnormal/(n) Examination			
Occupational Category	Group	1985	1987	1992	1997
All	***Ranch Hand***	***30 (3.7) (802)***	***35 (4.5) (777)***	***39 (5.0) (777)***	***55 (6.9) (802)***
	Comparison	***21 (2.0) (1,048)***	***43 (4.2) (1,018)***	***31 (3.1) (1,014)***	***59 (5.6) (1,048)***
Officer	Ranch Hand	8 (2.6) (308)	11 (3.6) (302)	13 (4.3) (301)	17 (5.5) (308)
	Comparison	7 (1.7) (414)	11 (2.7) (403)	16 (4.0) (404)	23 (5.6) (414)
Enlisted Flyer	Ranch Hand	5 (3.4) (146)	7 (4.9) (143)	5 (3.5) (142)	13 (8.9) (146)
	Comparison	1 (0.6) (156)	7 (4.7) (150)	3 (2.0) (154)	8 (5.1) (156)
Enlisted Groundcrew	Ranch Hand	17 (4.9) (348)	17 (5.1) (332)	21 (6.3) (334)	25 (7.2) (348)
	Comparison	13 (2.7) (478)	25 (5.4) (465)	12 (2.6) (456)	28 (5.9) (478)

Table 11-37. Longitudinal Analysis of Cranial Nerve Index (Continued)

Occupational Category	Group	Normal in 1985: n in 1997	Normal in 1985: Number (%) Abnormal in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***772***	***41 (5.3)***	***1.05 (0.69,1.59)***	***0.836***
	Comparison	***1,027***	***52 (5.1)***		
Officer	Ranch Hand	300	16 (5.3)	1.20 (0.60,2.39)	0.613
	Comparison	407	18 (4.4)		
Enlisted Flyer	Ranch Hand	141	9 (6.4)	1.23 (0.46,3.28)	0.684
	Comparison	155	8 (5.2)		
Enlisted Groundcrew	Ranch Hand	331	16 (4.8)	0.89 (0.47,1.68)	0.710
	Comparison	465	26 (5.6)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1985 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1985, 1992, and 1997 examinations. Statistical analyses are based only on participants with a normal cranial nerve index in 1985 (see Chapter 7, Statistical Methods).

(b) MODEL 2: RANCH HANDS – INITIAL DIOXIN

Initial Dioxin	Number (%) Abnormal/(n) Examination: 1985	1987	1992	1997
Low	3 (2.0) (148)	6 (4.1) (147)	9 (6.3) (142)	13 (8.8) (148)
Medium	5 (3.1) (159)	10 (6.5) (154)	4 (2.6) (155)	9 (5.7) (159)
High	5 (3.4) (146)	5 (3.6) (140)	9 (6.4) (141)	7 (4.8) (146)

Initial Dioxin Category Summary Statistics: Initial Dioxin	Normal in 1985: n in 1997	Normal in 1985: Number (%) Abnormal in 1997	Analysis Results for Log_2 (Initial Dioxin)[a]: Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	145	12 (8.3)	0.66 (0.42,1.03)	0.049
Medium	154	5 (3.3)		
High	141	4 (2.8)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1985, 1992, and 1997 examinations. Statistical analyses are based only on participants with a normal cranial nerve index in 1985 (see Chapter 7, Statistical Methods).

Table 11-37. Longitudinal Analysis of Cranial Nerve Index (Continued)

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY				
	Number (%) Abnormal/(n) Examination			
Dioxin Category	**1985**	**1987**	**1992**	**1997**
Comparison	20 (2.0) (1,019)	43 (4.3) (991)	30 (3.0) (987)	56 (5.5) (1,019)
Background RH	17 (5.0) (343)	14 (4.2) (330)	17 (5.1) (333)	25 (7.3) (343)
Low RH	7 (3.1) (224)	13 (5.9) (220)	12 (5.6) (215)	19 (8.5) (224)
High RH	6 (2.6) (229)	8 (3.6) (221)	10 (4.5) (223)	10 (4.4) (229)
Low plus High RH	13 (2.9) (453)	21 (4.8) (441)	22 (5.0) (438)	29 (6.4) (453)

	Normal in 1985			
Dioxin Category	**n in 1997**	**Number (%) Abnormal in 1997**	**Adj. Relative Risk (95% C.I.)[ab]**	**p-Value[b]**
Comparison	999	50 (5.0)		
Background RH	326	19 (5.8)	1.21 (0.70,2.10)	0.496
Low RH	217	15 (6.9)	1.29 (0.71,2.35)	0.410
High RH	223	6 (2.7)	0.54 (0.23,1.29)	0.167
Low plus High RH	440	21 (4.8)	0.83 (0.47,1.47)	0.522

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1985, 1992, and 1997 examinations. Statistical analyses are based only on participants with a normal cranial nerve index in 1985 (see Chapter 7, Statistical Methods).

The Model 2 longitudinal analysis revealed an inverse significant relation between initial dioxin and the cranial nerve index (Table 11-37(b): Adj. RR=0.66, p=0.049). As initial dioxin increased, the prevalence of an abnormal cranial nerve index decreased.

All results from the Model 3 longitudinal analysis of cranial nerve index were nonsignificant (Table 11-37(c): p>0.16 for each Model 3 contrast).

11.2.3.1.2 CNS Index

Based on participants with a normal CNS index in 1985, all results from the longitudinal analysis of the CNS index for Models 1 through 3 were nonsignificant (Table 11-38(a–c): p>0.20 for each analysis).

Table 11-38. Longitudinal Analysis of CNS Index

(a) MODEL 1: RANCH HANDS VS. COMPARISONS					
		Number (%) Abnormal/(n) Examination			
Occupational Category	Group	1985	1987	1992	1997
All	***Ranch Hand***	***29 (3.5) (826)***	***44 (5.5) (805)***	***39 (4.9) (804)***	***105 (12.7) (826)***
	Comparison	***27 (2.6) (1,060)***	***45 (4.4) (1,034)***	***50 (4.8) (1,033)***	***128 (12.1) (1,060)***
Officer	Ranch Hand	7 (2.2) (322)	10 (3.2) (316)	15 (4.8) (316)	38 (11.8) (322)
	Comparison	5 (1.2) (420)	17 (4.2) (410)	24 (5.8) (413)	47 (11.2) (420)
Enlisted Flyer	Ranch Hand	7 (4.8) (146)	6 (4.2) (143)	8 (5.6) (144)	24 (16.4) (146)
	Comparison	7 (4.4) (159)	5 (3.2) (155)	2 (1.3) (157)	21 (13.2) (159)
Enlisted Groundcrew	Ranch Hand	15 (4.2) (358)	28 (8.1) (346)	16 (4.7) (344)	43 (12.0) (358)
	Comparison	15 (3.1) (481)	23 (4.9) (469)	24 (5.2) (463)	60 (12.5) (481)

		Normal in 1985			
Occupational Category	Group	n in 1997	Number (%) Abnormal in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***797***	***90 (11.3)***	***1.05 (0.78,1.42)***	***0.725***
	Comparison	***1,033***	***111 (10.8)***		
Officer	Ranch Hand	315	34 (10.8)	0.99 (0.61,1.59)	0.955
	Comparison	415	45 (10.8)		
Enlisted Flyer	Ranch Hand	139	21 (15.1)	1.59 (0.78,3.24)	0.201
	Comparison	152	15 (9.9)		
Enlisted Groundcrew	Ranch Hand	343	35 (10.2)	0.95 (0.60,1.51)	0.835
	Comparison	466	51 (10.9)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1985, 1992, and 1997 examinations. Statistical analyses are based only on participants with a normal CNS index in 1985 (see Chapter 7, Statistical Methods).

Table 11-38. Longitudinal Analysis of CNS Index (Continued)

(b) MODEL 2: RANCH HANDS – INITIAL DIOXIN				
	Number (%) Abnormal/(n) Examination			
Initial Dioxin	1985	1987	1992	1997
Low	7 (4.6) (153)	4 (2.6) (153)	6 (4.1) (148)	18 (11.8) (153)
Medium	4 (2.5) (159)	8 (5.1) (156)	8 (5.2) (155)	21 (13.2) (159)
High	4 (2.7) (151)	10 (6.8) (147)	4 (2.7) (147)	15 (9.9) (151)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1985			
Initial Dioxin	n in 1997	Number (%) Abnormal in 1997	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	146	15 (10.3)	1.13 (0.89,1.42)	0.319
Medium	155	20 (12.9)		
High	147	14 (9.5)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1985, 1992, and 1997 examinations. Statistical analyses are based only on participants with a normal CNS index in 1985 (see Chapter 7, Statistical Methods).

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY				
	Number (%) Abnormal/(n) Examination			
Dioxin Category	1985	1987	1992	1997
Comparison	26 (2.5) (1,031)	44 (4.4) (1,007)	49 (4.9) (1,006)	126 (12.2) (1,031)
Background RH	14 (3.9) (357)	21 (6.1) (343)	20 (5.8) (348)	50 (14.0) (357)
Low RH	7 (3.1) (229)	6 (2.6) (227)	9 (4.1) (221)	24 (10.5) (229)
High RH	8 (3.4) (234)	16 (7.0) (229)	9 (3.9) (229)	30 (12.8) (234)
Low plus High RH	15 (3.2) (463)	22 (4.8) (456)	18 (4.0) (450)	54 (11.7) (463)

Table 11-38. Longitudinal Analysis of CNS Index (Continued)

Dioxin Category	Normal in 1985: n in 1997	Normal in 1985: Number (%) Abnormal in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	1,005	110 (11.0)		
Background RH	343	40 (11.7)	1.07 (0.72,1.58)	0.749
Low RH	222	21 (9.5)	0.76 (0.46,1.25)	0.279
High RH	226	28 (12.4)	1.31 (0.83,2.06)	0.244
Low plus High RH	448	49 (10.9)	1.00 (0.69,1.44)	0.999

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1985, 1992, and 1997 examinations. Statistical analyses are based only on participants with a normal CNS index in 1985 (see Chapter 7, Statistical Methods).

11.3 DISCUSSION

The data analyzed in the neurological assessment can be relied upon to detect the presence, if not the cause, of neurological disease, including disorders of the peripheral nervous system. CNS, cranial, and peripheral nerve variables examined can provide specific clues to the anatomical site of neurological lesions and clarify the need for additional diagnostic studies. Pertinent to the current study, the neurological examination is highly sensitive in detecting the presence of peripheral neuropathy, a suspected clinical condition related to herbicide exposure.

In clinical practice, it is convenient to divide the neurological assessment into examinations of the peripheral and cranial nerves. The motor and sensory peripheral nerve variables and the cranial nerve variables examined provide highly specific clues to the anatomic site of neurological lesions and clarify which additional diagnostic studies would be most helpful in establishing a diagnosis. As indices of CNS function, tremor and coordination are less specific and more subject to individual variation in the absence of underlying neurological disease. Tremor, for example, may occur as a benign familial trait, may be reflective of alcohol withdrawal, or may be a marker of extra-pyramidal motor system disease as in Parkinson's syndrome. The Romberg sign may signal a lesion in the cerebellum but is more often indicative of impaired position sense in the lower extremities or of inner ear disease. Finally, the mental status examination is of obvious importance in the CNS assessment and, as in previous AFHS examinations, extensive psychometric studies were conducted and are reported in Chapter 12, Psychology Assessment.

Analysis of inflammatory diseases confirmed by a medical records review found a significant excess among Ranch Hands (n=7 or 0.8%) relative to Comparisons (n=1 or 0.1%). Of the seven Ranch Hands with inflammatory diseases, three (42.9%) had meningitis caused by bacterial infections. The single Comparison with an inflammatory disease had encephalitis of unknown cause, suggesting that this

finding is unrelated to herbicide or dioxin exposure. Consistent with the 1987 and 1992 examinations, Ranch Hands with low and high levels of categorized dioxin were more likely than Comparisons to develop other neurological disorders, although the associations were not significant after adjustment for covariates. Similar results were noted with respect to 1987 serum dioxin levels. Although the prevalence of peripheral neurological disorders established by a medical records review was similar in Ranch Hands and Comparisons (21.8% and 19.3%, respectively), there was evidence for an association with dioxin levels in two of the models. Ranch Hands in the low plus high dioxin category were at significantly greater risk than Comparisons (25.1% versus 19.3%, respectively), a contrast that remained marginally significant after adjustment for covariates. Further, in both the unadjusted and adjusted analyses, a significant positive association was noted between the occurrence of peripheral disorders and 1987 dioxin levels.

With one exception, no significant associations were noted in the analyses of any of the directly measured physical examination variables. Ranch Hands were significantly more likely than Comparisons to develop restricted range of motion at the neck, a common occurrence in any aging population and one that is usually related to osteoarthritis of the cervical spine rather than any primary neurological cause. Across occupational strata, the contrast was significant only in the enlisted flyer category. Ranch Hands with low and high levels of categorized dioxin were at significantly greater risk for the development of restricted neck range of motion.

Only one of the analyses of peripheral motor and sensory nerve function yielded significant group differences. By inspection and palpation, Ranch Hands were more likely than Comparisons to have abnormalities of muscle mass (4.5% versus 3.0%, respectively) particularly in the enlisted groundcrew occupational category (4.3% versus 2.1%), even after adjustment for covariates. In none of the individual analyses was there any significant associations with 1987 serum dioxin levels, nor were any group differences detected in the analyses of CNS coordination variables.

Significant group differences were found in three of the four composite polyneuropathy indices described earlier in this chapter. Ranch Hands were significantly more likely than Comparisons to have abnormalities in the confirmed polyneuropathy index (1.4% versus 0.6%), the polyneuropathy severity index of moderate degree (2.6% versus 1.1%), and the multiple polyneuropathy index (5.0% versus 3.2%). In each case, Ranch Hands in the high dioxin category were at a significantly greater risk for abnormal scores than Comparisons; the prevalence of abnormalities increased as initial dioxin increased.

Longitudinal analyses conducted during 12 years of observation yielded no significant differences between the Ranch Hand and Comparison cohorts, nor was there any evidence for dose responses with respect to either initial or 1987 dioxin levels.

Dependent variable-covariate analyses confirmed associations with age and diabetes that are well established. Diabetes was by far the strongest covariate and significantly associated with neurological disease historically, on physical examination, and as assessed by all of the composite indices. Associations with alcohol were sporadic and less prominent than during previous AFHS examinations.

In summary, in contrast to previous examinations, the history of neurological disease now appears significantly greater in Ranch Hands than Comparisons historically (diseases of inflammatory origin and peripheral disorders), on physical examination (restriction of range of motion), and as reflected in several of the composite indices described above. Further, the associations of neck range of motion with categorized dioxin and a history of peripheral disorders with 1987 dioxin provide evidence of an

association of neurological disease with prior exposure to dioxin. The results of the analysis of the polyneuropathy indices also provide support of an association between dioxin and neurological disease.

11.4 SUMMARY

Four neurological disorders, which were verified by a medical records review, and extensive physical examination data on cranial nerve function, peripheral nerve status, and CNS coordination processes were analyzed in the neurological assessment. Each endpoint was examined for a significant association, both unadjusted and adjusted for covariates, with group (Model 1), initial dioxin (Model 2), categorized dioxin (Model 3), and 1987 dioxin levels (Model 4). Summaries of the Model 1 through 4 analyses are tabled and discussed below, with emphasis on significant findings from the adjusted analysis.

11.4.1 Model 1: Group Analysis

The prevalence of inflammatory diseases, a restricted neck range of motion, and a moderate polyneuropathy severity index was significantly greater for Ranch Hands than for Comparisons when combining all occupations. Significantly more Comparisons than Ranch Hands had an abnormal light reaction. Other neurological disorders, the multiple polyneuropathy index, the confirmed polyneuropathy index, and muscle status showed a marginally significant increase in all Ranch Hands relative to Comparisons. No significant differences were observed between Ranch Hand and Comparison officers. The neck range of motion and moderate polyneuropathy severity index results were significant or marginally significant in the contrast of Ranch Hand and Comparison enlisted flyers. The confirmed polyneuropathy indicator and muscle status results were significant or marginally significant in the enlisted groundcrew. Table 11-39 displays the Model 1 results of all unadjusted and adjusted analyses.

Table 11-39. Summary of Group Analysis (Model 1) for Neurology Variables (Ranch Hands vs. Comparisons)

	UNADJUSTED			
Variable	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Medical Records				
Inflammatory Diseases	+0.006	NS	NS	NS
Hereditary and Degenerative Diseases	NS	NS	NS	ns
Peripheral Disorders	NS	NS	NS	NS
Other Neurological Disorders	NS*	NS	NS	NS
Physical Examination				
Smell	NS	ns	NS*	NS
Visual Fields	ns	ns	ns	ns
Light Reaction	-0.007	ns	ns	ns
Ocular Movement	NS	ns	NS	NS
Facial Sensation	NS	NS	ns	NS
Jaw Clench	NS	NS	--	--
Smile	NS	ns	NS	NS
Palpebral Fissure	ns	ns	NS	NS
Balance	NS	NS	ns	ns
Speech	ns	ns	ns	ns
Tongue Position Relative to Midline	NS	NS	--	--
Palate and Uvula Movement	NS	NS	--	--

Table 11-39. Summary of Group Analysis (Model 1) for Neurology Variables (Ranch Hands vs. Comparisons) (Continued)

Variable	UNADJUSTED All	Officer	Enlisted Flyer	Enlisted Groundcrew
Cranial Nerve Index	NS	ns	NS	NS
Neck Range of Motion	+0.016	NS	+0.009	NS
Pinprick	NS	NS	NS	ns
Light Touch	NS	NS	NS	ns
Muscle Status	NS*	NS	NS	NS*
Patellar Reflex	ns	NS	ns*	NS
Achilles Reflex	NS	NS	NS	NS
Biceps Reflex	NS	NS	NS	NS
Babinski Reflex	ns	NS	ns	ns
Polyneuropathy Severity Index				
Moderate vs. None/Mild	+0.015	NS	NS*	NS
Severe vs. None/Mild	NS	NS	--	NS
Polyneuropathy Prevalence Index	NS	NS	ns	NS
Multiple Polyneuropathy Index	+0.046	NS	NS	NS
Confirmed Polyneuropathy Indicator	NS*	ns	NS*	NS*
Tremor	ns	NS	NS	ns
Coordination	ns	NS	ns	ns
Romberg Sign	NS	NS	ns	ns
Gait	NS	NS	NS	NS
CNS Index	NS	NS	NS	ns

Note: NS or ns: Not significant (p>0.10).
NS* or ns*: Marginally significant (0.05<p≤0.10).
+: Relative risk ≥1.00.
-: Relative risk <1.00.
--: Analysis not performed because of the sparse number of participants with an abnormality.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater. A lowercase "ns" denotes a relative risk less than 1.00.

Variable	ADJUSTED All	Officer	Enlisted Flyer	Enlisted Groundcrew
Medical Records				
Inflammatory Diseases	+0.002	--	--	NS
Hereditary and Degenerative Diseases	NS	NS	NS	ns
Peripheral Disorders	NS	NS	ns	NS
Other Neurological Disorders	NS*	NS	NS	NS
Physical Examination				
Smell	NS	ns	NS	NS
Visual Fields	ns	--	ns	ns
Light Reaction	-0.010	--	ns	--
Ocular Movement	NS	ns	NS	NS
Facial Sensation	NS	NS	--	--
Jaw Clench	--	--	--	--
Smile	NS	ns	--	NS
Palpebral Fissure	ns	ns	ns	ns

Table 11-39. Summary of Group Analysis (Model 1) for Neurology Variables (Ranch Hands vs. Comparisons) (Continued)

Variable	ADJUSTED All	Officer	Enlisted Flyer	Enlisted Groundcrew
Balance	NS	NS	--	ns
Speech	ns	ns	--	ns
Tongue Position Relative to Midline	--	--	--	--
Palate and Uvula Movement	--	--	--	--
Cranial Nerve Index	NS	ns	NS	NS
Neck Range of Motion	+0.015	NS	+0.016	NS
Pinprick	NS	NS	NS	ns
Light Touch	NS	NS	NS	ns
Muscle Status	NS*	ns	NS	+0.046
Patellar Reflex	ns	NS	ns*	NS
Achilles Reflex	NS	NS	ns	NS
Biceps Reflex	NS	NS	NS	NS
Babinski Reflex	ns	NS	ns	ns
Polyneuropathy Severity Index				
Moderate vs. None/Mild	+0.020	NS	NS*	NS
Severe vs. None/Mild	NS	--	--	NS
Polyneuropathy Prevalence Index	ns	NS	ns	NS
Multiple Polyneuropathy Index	NS*	NS	NS	NS
Confirmed Polyneuropathy Indicator	NS*	ns	--	NS*
Tremor	ns	NS	NS	ns
Coordination	ns	NS	ns	ns
Romberg Sign	NS	NS	--	ns
Gait	NS	NS	NS	NS*
CNS Index	ns	NS	ns	NS

Note: NS or ns: Not significant (p>0.10).
NS* or ns*: Marginally significant (0.05<p≤0.10).
+: Relative risk ≥1.00.
-: Relative risk <1.00.
--: Analysis not performed because of the sparse number of participants with an abnormality.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater. A lowercase "ns" denotes a relative risk less than 1.00.

11.4.2 Model 2: Initial Dioxin Analysis

Table 11-40 summarizes the results from the Model 2 analyses. Several positive and significant associations between the neurological variables and initial dioxin were found in adjusted analyses. In assessing the cranial nerve function, abnormal visual fields increased as initial dioxin increased. The assessment of measures of peripheral nerve status showed a significant or marginally significant positive association between initial dioxin and the patellar and Achilles reflexes. An association between all four polyneuropathy indices and dioxin was observed. The moderate classification of the polyneuropathy severity index, the polyneuropathy prevalence index, the multiple polyneuropathy index, and the confirmed polyneuropathy indicator were all significant and positively associated with initial dioxin.

Table 11-40. Summary of Initial Dioxin Analysis (Model 2) for Neurology Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Inflammatory Diseases	NS	ns
Hereditary and Degenerative Diseases	NS	NS
Peripheral Disorders	NS	NS
Other Neurological Disorders	NS	ns
Physical Examination		
Smell	ns	ns
Visual Fields	+0.040	+0.049
Light Reaction	--	--
Ocular Movement	ns	ns
Facial Sensation	ns	ns
Jaw Clench	ns	ns
Smile	NS	NS
Palpebral Fissure	NS	NS
Balance	NS	NS
Speech	ns	ns*
Tongue Position Relative to Midline	ns	ns
Palate and Uvula Movement	ns	ns
Cranial Nerve Index	ns	ns
Neck Range of Motion	ns*	ns
Pinprick	NS	NS
Light Touch	ns	NS
Muscle Status	ns	ns
Patellar Reflex	NS	+0.019
Achilles Reflex	NS	NS*
Biceps Reflex	ns	ns
Babinski Reflex	ns	NS
Polyneuropathy Severity Index		
Moderate vs. None/Mild	NS	+0.042
Severe vs. None/Mild	ns	ns
Polyneuropathy Prevalence Index	NS	+0.029
Multiple Polyneuropathy Index	NS*	+0.004
Confirmed Polyneuropathy Indicator	+0.033	+0.008
Tremor	NS	NS
Coordination	ns	NS
Romberg Sign	NS	NS
Gait	NS	NS
CNS Index	NS	NS

Note: NS or ns: Not significant ($p>0.10$).
NS* or ns*: Marginally significant ($0.05<p\leq0.10$).
+: Relative risk $\geq$1.00.
--: Analysis not performed because of the sparse number of participants with an abnormality.

P-value given if $p\leq0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater. A lowercase "ns" denotes a relative risk less than 1.00.

11.4.3 Model 3: Categorized Dioxin Analysis

Results from the Model 3 analyses of the neurology variables are presented in Table 11-41. Each significant or marginally significant result from the Model 3 adjusted analyses displayed more Ranch Hands than Comparisons with a neurological abnormality. The adjusted analysis of inflammatory diseases displayed significant results for all levels of categorized dioxin. Results for peripheral disorders showed a marginally significant increased prevalence in the low plus high Ranch Hand dioxin category after adjustment for covariates. Neck range of motion was significantly greater for Ranch Hands in the low, high, and low plus high dioxin categories than for Comparisons. An increased prevalence of an abnormal muscle status was observed in the low and low plus high Ranch Hand dioxin categories. A marginally significant increase in an abnormal biceps reflex also was found for Ranch Hands in the low dioxin category. The polyneuropathy severity index showed an increase in the moderate classification of severity for Ranch Hands in the low, high, and low plus high dioxin categories. An increase in the severe classification of the polyneuropathy index was found for Ranch Hands in the low plus high dioxin category. Significant results also were found for Ranch Hands in the high dioxin category for the multiple polyneuropathy index and the confirmed polyneuropathy indicator. The prevalence of an abnormal confirmed polyneuropathy indicator was significantly greater for the low plus high Ranch Hand dioxin category than for Comparisons.

Table 11-41. Summary of Categorized Dioxin Analysis (Model 3) for Neurology Variables (Ranch Hands vs. Comparisons)

	UNADJUSTED			
Variable	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Medical Records				
Inflammatory Diseases	NS*	NS*	NS*	+0.035
Hereditary and Degenerative Diseases	NS	NS	NS	NS
Peripheral Disorders	ns	+0.033	NS*	+0.014
Other Neurological Disorders	ns	+0.023	+0.005	+0.001
Physical Examination				
Smell	NS	NS	NS	NS
Visual Fields	ns	ns	ns	ns
Light Reaction	ns	ns	ns	ns*
Ocular Movement	ns	NS	NS	NS
Facial Sensation	NS	NS	ns	NS
Jaw Clench	NS	NS	--	NS
Smile	NS	NS	NS	NS
Palpebral Fissure	NS	ns	ns	ns
Balance	NS	ns	ns	ns
Speech	ns	NS	ns	ns
Tongue Position Relative to Midline	NS	NS	--	NS
Palate and Uvula Movement	--	NS	--	NS
Cranial Nerve Index	NS	NS	ns	NS
Neck Range of Motion	NS	+0.002	NS	+0.003
Pinprick	NS	NS	NS*	NS
Light Touch	NS	NS	NS	NS
Muscle Status	NS	+0.021	NS	+0.033
Patellar Reflex	ns	NS	NS	NS
Achilles Reflex	ns	NS	NS	NS
Biceps Reflex	ns	+0.029	NS	NS

Table 11-41. Summary of Categorized Dioxin Analysis (Model 3) for Neurology Variables (Ranch Hands vs. Comparisons) (Continued)

Variable	UNADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Babinski Reflex	NS	ns	ns	ns
Polyneuropathy Severity Index				
Moderate vs. None/Mild	NS	+0.032	+0.042	+0.011
Severe vs. None/Mild	NS	NS*	NS	NS*
Polyneuropathy Prevalence Index	ns	NS	NS	NS
Multiple Polyneuropathy Index	NS	NS	+0.018	+0.042
Confirmed Polyneuropathy Indicator	NS	NS	+0.017	+0.047
Tremor	NS	ns	ns	ns
Coordination	NS	ns	ns	ns
Romberg Sign	NS	ns	ns	ns
Gait	NS	ns	NS	NS
CNS Index	NS	ns	NS	ns

Note: NS or ns: Not significant (p>0.10).
NS* or ns*: Marginally significant (0.05<p≤0.10).
+: Relative risk ≥1.00.
--: Analysis not performed because of the sparse number of participants with an abnormality.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater. A lowercase "ns" denotes a relative risk less than 1.00.

Variable	ADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Medical Records				
Inflammatory Diseases	+0.029	+0.035	+0.047	+0.024
Hereditary and Degenerative Diseases	NS	ns	NS	ns
Peripheral Disorders	ns	NS	NS	NS*
Other Neurological Disorders	NS	NS	NS	NS
Physical Examination				
Smell	NS	NS	ns	NS
Visual Fields	ns	--	ns	--
Light Reaction	ns	--	--	--
Ocular Movement	NS	NS	NS	NS
Facial Sensation	NS	NS	--	--
Jaw Clench	--	--	--	--
Smile	NS	NS	NS	NS
Palpebral Fissure	ns	ns	ns	ns
Balance	NS	ns	ns	ns
Speech	NS	NS	--	--
Tongue Position Relative to Midline	--	--	--	--
Palate and Uvula Movement	--	--	--	--

Table 11-41. Summary of Categorized Dioxin Analysis (Model 3) for Neurology Variables (Ranch Hands vs. Comparisons) (Continued)

	ADJUSTED			
Variable	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Cranial Nerve Index	NS	NS	ns	ns
Neck Range of Motion	NS	+0.010	+0.028	+0.002
Pinprick	NS	ns	NS	NS
Light Touch	NS	NS	NS	NS
Muscle Status	NS	NS*	NS	NS*
Patellar Reflex	ns	ns	NS	NS
Achilles Reflex	ns	ns	NS	NS
Biceps Reflex	ns	NS*	NS	NS
Babinski Reflex	NS	ns	ns	ns
Polyneuropathy Severity Index				
Moderate vs. None/Mild	NS	NS*	+0.024	+0.014
Severe vs. None/Mild	NS	NS	NS	NS*
Polyneuropathy Prevalence Index	ns	ns	NS	NS
Multiple Polyneuropathy Index	NS	ns	+0.016	NS
Confirmed Polyneuropathy Indicator	ns	NS	+0.007	+0.047
Tremor	NS	ns	ns	ns
Coordination	NS	ns	ns	ns
Romberg Sign	NS	ns	ns	ns
Gait	NS	ns	NS	NS
CNS Index	NS	ns	ns	ns

Note: NS or ns: Not significant (p>0.10).
NS*: Marginally significant (0.05<p≤0.10).
+: Relative risk ≥1.00.
--: Analysis not performed because of the sparse number of participants with an abnormality.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater. A lowercase "ns" denotes a relative risk less than 1.00.

11.4.4 Model 4: 1987 Dioxin Analysis

Significant positive associations were found between 1987 dioxin and peripheral disorders, the moderate classification of the polyneuropathy severity index, and the confirmed polyneuropathy indicator. A marginally significant positive association between the polyneuropathy prevalence index and 1987 dioxin was found. Complete Model 4 analysis results are presented in Table 11-42.

Table 11-42. Summary of 1987 Dioxin Analysis (Model 4) for Neurology Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Inflammatory Diseases	ns	ns
Hereditary and Degenerative Diseases	ns	ns
Peripheral Disorders	+0.010	+0.011
Other Neurological Disorders	+0.038	ns
Physical Examination		
Smell	ns	ns
Visual Fields	NS	NS
Light Reaction	ns	ns
Ocular Movement	NS	ns
Facial Sensation	ns	ns
Jaw Clench	ns	NS
Smile	NS	ns
Palpebral Fissure	NS	NS
Balance	ns	ns
Speech	ns	ns
Tongue Position Relative to Midline	ns	NS
Palate and Uvula Movement	NS	NS
Cranial Nerve Index	ns	ns
Neck Range of Motion	NS	NS
Pinprick	NS	NS
Light Touch	NS	NS
Muscle Status	NS	ns
Patellar Reflex	NS	NS
Achilles Reflex	NS	NS
Biceps Reflex	NS	NS
Babinski Reflex	ns*	ns
Polyneuropathy Severity Index		
Moderate vs. None/Mild	+0.024	+0.013
Severe vs. None/Mild	NS	NS
Polyneuropathy Prevalence Index	NS	NS*
Multiple Polyneuropathy Index	NS	NS
Confirmed Polyneuropathy Indicator	+0.002	+0.003
Tremor	ns	ns
Coordination	ns	ns
Romberg Sign	ns	ns
Gait	NS	ns
CNS Index	ns	ns

Table 11-42. Summary of 1987 Dioxin Analysis (Model 4) for Neurology Variables (Ranch Hands Only) (Continued)

Note: NS or ns: Not significant (p>0.10).
NS* or ns*: Marginally significant (0.05<p≤0.10).
+: Relative risk ≥1.00.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater. A lowercase "ns" denotes a relative risk less than 1.00.

11.5 CONCLUSION

Four neurological disorders and extensive physical examination data on cranial nerve function, peripheral nerve status, and CNS coordination processes were analyzed in the neurological assessment. Inflammatory diseases verified by a medical records review found a significant excess among Ranch Hands (n=7) relative to Comparisons (n=1); however, three of the seven Ranch Hand diseases were caused by bacterial infections, suggesting that this finding is unrelated to herbicide or dioxin exposure. Peripheral disorders, as verified by a medical records review, increased in Ranch Hands as levels of 1987 dioxin increased. Neck range of motion abnormalities were increased in Ranch Hands relative to Comparisons in terms of both a group designation and categorized dioxin levels. The increase in abnormalities for Ranch Hands relative to Comparisons was noted in enlisted flyers. An increase in the risk of an abnormal muscle status was observed in Ranch Hand enlisted groundcrew. A significant association between initial dioxin and both visual field and patellar reflex abnormalities was observed. Indices of polyneuropathy showed an increase in the prevalence of abnormality in Ranch Hands relative to Comparisons and a positive association with initial and 1987 dioxin levels. The clinical importance of the increased risk of polyneuropathy is uncertain due to the small number of affected veterans.

In summary, although a common etiology in these findings is not apparent, a statistically significant increase in neurological disease appears in Ranch Hands historically, on physical examination, and as reflected in several of the composite polyneuropathy indices. Further, the associations of neck range of motion abnormalities with categorized dioxin and a history of peripheral disorders with 1987 dioxin provide evidence of an association of neurological disease with elevated dioxin levels. The results of the analysis of the polyneuropathy indices also provide support of an association between elevated dioxin levels and neurological disease; however, the clinical importance of this finding is uncertain.

REFERENCES

1. Mohammad, F. K., and V. E. V. St. Omer. 1986. Behavioral and developmental effects in rats following in utero exposure to 2,4-D/2,4,5-T mixture. *Neurobehavioral Toxicology and Teratology* 8:551-60.

2. Mohammad, F. K., and V. E. V. St. Omer. 1988. Behavioral and neurochemical alterations in rats prenatally exposed to 2,4-dichlorophenoxyacetate (2,4-D) and 2,4,5-trichlorophenoxyacetate (2,4,5-T) mixture. *Teratology* 37:515.

3. St. Omer, V. E. V., and F. K. Mohammad. 1987. Ontogeny of swimming behavior and brain catecholamine turnover in rats prenatally exposed to a mixture of 2,4-D and 2,4,5-T. *Neuropharmacology* 26:1351-8.

4. Kim, C. S., R. F. Keizer, and J. B. Pritchard. 1988. 2,4-dichlorophenoxyacetic acid intoxication increases its accumulation within the brain. *Brain Research* 440:216-26.

5. Schulze, G. E., and J. A. Dougherty. 1988. Neurobehavioral toxicity of 2,4-D-n-butyl ester (2,4-D ester): Tolerance and lack of cross-tolerance. *Neurotoxicology and Teratology* 10:75-9.

6. Schulze, G. E., and J. A. Dougherty. 1988. Neurobehavioral toxicity and tolerance to the herbicide 2,4-dichlorophenoxyacetic and acid-n-butyl ester (2,4-D ester). *Fundamental and Applied Toxicology* 10:413-24.

7. Sirkka, U., R. Pohjanvirta, S. A. Nieminen, J. Tuomisto, and P. Ylitalo. 1992. Acute neurobehavioral effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in Han/Wistar rats. *Pharmacology and Toxicology* 71:284-8.

8. Pohjanvirta, R., L. Tuomisto, and J. Tuomisto. 1989. The central nervous system may be involved in TCDD toxicity. *Toxicology* 58:167-74.

9. Silbergeld, E. K., and S. R. Max. 1986. Neuromuscular targets for the action of 2,3,7,8-TCDD. Abstract of a paper presented at the 6th International Symposium on Chlorinated Dioxins and Related Compounds, September 16-19, Fukuoka, Japan.

10. Grahmann, F., D. Claus, H. Grehl, and B. Neundorfer. 1993. Electrophysiologic evidence for a toxic polyneuropathy in rats after exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Journal of the Neurological Sciences* 115(1):71-5.

11. Grehl, H., F. Grahmann, D. Claus, and B. Neundorfer. 1993. Histologic evidence for a toxic polyneuropathy due to exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in rats. *Acta Neurologica Scandinavica* 88:354-7.

12. Mattsson, J. L., and D. L. Eisenbrandt. 1990. The improbable association between the herbicide 2,4-D and polyneuropathy. *Biomedical and Environmental Sciences* 3:43-51.

13. Seabury, J. H. 1963. Toxicity of 2,4-dichlorophenoxyacetic acid. *Archives of Environmental Health* 7:202-9.

14. Klawans, H. L. 1987. Dystonia and tremor following exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Movement Disorders* 2:255-61.

15. Oliver, R. M. 1975. Toxic effects of 2,3,7,8-tetrachlorodibenzo-1,4-dioxin in laboratory workers. *British Journal of Industrial Medicine* 32:49-53.

16. Singer, R., M. Moses, J. Valciukas, R. Lilis, and I. J. Selikoff. 1982. Nerve conduction velocity studies of workers employed in the manufacture of phenoxy herbicides. *Environmental Research* 29:297-311.

17. Moses, M., R. Lilis, K. D. Crow, J. Thornton, A. Fischbein, H. A. Anderson, and I. J. Selikoff. 1984. Health status of workers with past exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin in the manufacture of 2,4,5-trichlorophenoxyacetic acid: Comparison of findings with and without chloracne. *American Journal of Industrial Medicine* 5:161-82.

18. Suskind, R. R., and V. S. Hertzberg. 1984. Human health effects of 2,4,5-T and its toxic contaminants. *Journal of the American Medical Association* 251:2372-80.

19. Pazderova-Vejlupkova, J., M. Nemcova, J. Pickova, L. Jirasek, and E. Lukas. 1981. The development and prognosis of chronic intoxication by tetrachlorodibenzo-p-dioxin in men. *Archives of Environmental Health* 36:5-11.

20. Sweeney, M. H., M. A. Fingerhut, J. C. Arezzo, R. W. Hornung, and L. B. Connally. 1993. Peripheral neuropathy after occupational exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *American Journal of Industrial Medicine* 23:845-58.

21. Cheng, W. N., P. J. Coenraads, Z. H. Hao, and G. F. Liu. 1993. A health survey of workers in the pentachlorophenol section of a chemical manufacturing plant. *American Journal of Industrial Medicine* 24:81-92.

22. Webb, K. B., R. G. Evans, P. A. Stehr, and S. M. Ayres. 1987. Pilot study on health effects of environmental 2,3,7,8-TCDD in Missouri. *American Journal of Industrial Medicine* 11:685-91.

23. Webb, K. B., R. G. Evans, A. P. Knutsen, S. T. Roodman, D. W. Roberts, W. F. Schramm, B. B. Gibson, J. S. Andrews Jr., L. L. Needham, and D. G. Patterson. 1989. Medical evaluation of subjects with known body levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Journal of Toxicology and Environmental Health* 28:183-93.

24. Hoffman, R. E., P. A. Stehr-Green, K. B. Webb, R. G. Evans, A. P. Knutsen, W. F. Schramm, B. B. Gibson, and K. K. Steinberg. 1986. Health effects of long-term exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Journal of the American Medical Association* 225:2031-8.

25. Stehr, P. A., G. Stein, H. Falk, E. Sampson, S. J. Smith, K. Steinberg, K. Webb, S. Ayres, W. F. Schramm, H. D. Donnell, and W. B. Gedney. 1986. A pilot epidemiologic study of possible health effects associated with 2,3,7,8-tetrachlorodibenzo-p-dioxin contaminations in Missouri. *Archives of Environmental Health* 41:16-22.

26. Stehr-Green, P. A., J. S. Andrews Jr., R. E. Hoffman, K. B. Webb, and W. F. Schramm. 1988. An overview of the Missouri dioxin studies. *Archives of Environmental Health* 43:174-7.

27. Filippini, G., B. Bordo, P. Crenna, N. Massetto, M. Musicco, and R. Boeri. 1981. Relationship between clinical and electrophysiological findings and indicators of heavy exposure to 2,3,7,8-tetrachlorodibenzo-dioxin. *Scandinavian Journal of Work, Environment and Health* 7:257-62.

28. Bertazzi, P. A. 1991. Long-term effects of chemical disasters. Lessons and results from Seveso. *Science of the Total Environment* 196(1-2):5-20.

29. Boeri, R., B. Bordo, P. Crenna, G. Filippini, M. Massetto, and A. Zecchini. 1978. Preliminary results of a neurological investigation of the population exposed to TCDD in the Seveso region. *Rivista di Patologia Nervosa e Mentale* 99:111-28.

30. Barbieri, S., C. Pirovano, G. Scarlato, P. Tarchini, A. Zappa, and M. Maranzana. 1988. Long-term effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin on the peripheral nervous system. Clinical and neurophysiological controlled study on subjects with chloracne from the Seveso area. *Neuroepidemiology* 7:29-37.

31. Zober, A., M. G. Ott, and P. Messerer. 1994. Morbidity followup study of BASF employees exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) after a 1953 chemical reactor incident. *Occupational and Environmental Medicine* 51:479-86.

32. Assennato, G., D. Cervino, E. A. Emmett, G. Longo, and F. Merlo. 1989. Followup of subjects who developed chloracne following TCDD exposure at Seveso. *American Journal of Industrial Medicine* 16:119-25.

33. Morcarelli, P., A. Marocchi, P. Brambilla, P. Gerthoux, C. Beretta, L. Colombo, M. Bertona, C. Sarto, P. Tramacere, A. Mondonico, C. Crespi, S. Signorini, and R. Brivio. 1992. Human data derived from the Seveso accident, relevance for human risk assessment. *Toxic Substances Journal* 12(2-4):151-73.

34. Stellman, S. D., J. M. Stellman, and J. F. Sommer Jr. 1988. Health and reproductive outcomes among American Legionnaires in relation to combat and herbicide exposure in Vietnam. *Environmental Research* 47:150-74.

35. United States Centers for Disease Control. 1988. Health status of Vietnam veterans. II. Physical health. *Journal of the American Medical Association* 259:2708-14.

36. Lathrop, G. D., W. H. Wolfe, R. A. Albanese, and P. M. Moynahan. 1984. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Baseline Morbidity Study Results. NTIS: AD A-138-340. United States Air Force School of Aerospace Medicine, Brooks Air Force Base, Texas.

37. Lathrop, G. D., S. G. Machado, T. G. Karrison, W. D. Grubbs, W. F. Thomas, W. H. Wolfe, J. E. Michalek, J. C. Miner, and M. R. Peterson. 1987. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: First followup examination results. NTIS: AD A 188262. United States Air Force School of Aerospace Medicine, Brooks Air Force Base, Texas.

38. Thomas, W. F., W. D. Grubbs, T. G. Karrison, M. B. Lustik, R. H. Roegner, D. E. Williams, W. H. Wolfe, J. E. Michalek, J. C. Miner, and R. W. Ogershok. 1990. An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: I. 1987 followup examination results, May 1987 to January 1990. NTIS: AD A 222 573. United States Air Force School of Aerospace Medicine, Human Systems Division (AFSC), Brooks Air Force Base, Texas.

39. Grubbs, W. D., W. H. Wolfe, J. E. Michalek, D. E. Williams, M. B. Lustik, A. S. Brockman, S. C. Henderson, F. R. Burnett, R. G. Land, D. J. Osborne, V. K. Rocconi, M. E. Schreiber, J. C. Miner, G. L. Henriksen, and J. A. Swaby. 1995. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final Report. 1992 Followup Examination Results. NTIS: AD A 304 306, 304 308-316. United States Air Force School of Aerospace Medicine, Brooks Air Force Base, Texas.

40. Roegner, R. H., W. D. Grubbs, M. B. Lustik, A. S. Brockman, S. C. Henderson, D. E. Williams, W. H. Wolfe, J. E. Michalek, and J. C. Miner. 1991. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides. Serum dioxin analysis of 1987 examination results. NTIS: AD A 237 516-24. United States Air Force School of Aerospace Medicine, Brooks Air Force Base, Texas.

41. Institute of Medicine. 1999. *Veterans and Agent Orange: Update 1998.* National Academy Press: Washington, DC.

42. Gerr, F., D. Hershman, and R. Letz. 1990. Vibrotactile threshold measurement for detecting neurotoxicity: reliability and determination of age- and height-standardized normative values. *Archives of Environmental Health* 45:148-54.

43. Michalek, J. E., J. L. Pirkle, S. P. Caudill, R. C. Tripathi, D. G. Patterson Jr., and L. L. Needham. 1996. Pharmacokinetics of TCDD in Veterans of Operation Ranch Hand: 10-year Followup. *Journal of Toxicology and Environmental Health* 47:209-20.

44. Mausner, J. S., and A. K. Bahn. 1974. *Epidemiology – An Introductory Text.* Philadelphia: W. B. Saunders Company.

Table of Contents

List of Tables

12 PSYCHOLOGICAL ASSESSMENT

12.1 INTRODUCTION

12.1.1 Background

Signs of dioxin toxicity in animals (e.g., lethargy, stupor, poor coordination, lack of feeding, and agitation) have been observed in multiple studies in many species and have been attributed to the "wasting syndrome" of multi-organ toxicity rather than to primary central nervous system (CNS) involvement (1). Pharmacokinetic studies in rats (2), mice (3), and monkeys (4) have demonstrated that the blood brain barrier is relatively impermeable to dioxin, and experimental animal studies, therefore, provide little insight into the potential neuropsychological consequences of dioxin in humans.

In rats exposed to high doses of dioxin (1,000 micrograms intraperitoneally), only slight differences were noted in spontaneous motor activity and maze performance relative to controls (5). A more recent study from the same laboratory found no neurobehavioral impairment in rats given a sublethal dose of dioxin sufficient to cause the wasting syndrome (6). Experiments in monkeys have documented subtle behavioral dysfunction and cognitive impairment consequent to dioxin exposure in utero (7–10).

Using chloracne as a marker for high-level dioxin exposure, early studies of industrial chemical workers provided the first suggestion of associated psychological effects. Studies shortly after a Nitro, West Virginia, accident in 1949 documented nervousness, fatigue, irritability, cold intolerance, and decreased libido in many of the workers with chloracne. Most of these symptoms resolved over a 4-year period (11, 12). Two follow-up studies of expanded plant cohorts in 1979 noted a strong association between the occurrence of chloracne and insomnia (13, 14).

Other industrial-based studies reported a wide range of acute and subacute symptoms associated with exposure to chlorophenols. In addition to those cited above, impotence, reduced emotional responses, sensory deficits, reading difficulties, memory loss, and emotional instability have been described (15–20). Employing the Minnesota Multiphasic Personality Inventory (MMPI), one early study of chemical production workers found an association between the development of chloracne and hypomania and a significantly increased incidence of personality disorders in those most heavily exposed (19). Another report described marked personality changes in two of three chemists involved in the synthesis of dioxin (20). Yet another study of 55 Czechoslovakian workers found a significant incidence of anxiety and depression and of dementia associated with encephalopathy (7 percent) and neurasthenia (75 percent). Over a 10-year follow-up period, all symptoms of anxiety and depression had resolved (18).

Neuropsychiatric testing was included in the medical evaluations reported in two studies of 155 trailer park residents exposed to dioxin by contaminated soil in Quail Run, Missouri (21, 22). Relative to controls, exposed subjects had variations from the normal in the tension or anxiety and anger or hostility scales of the Profile of Mood States Inventory as well as in the vocabulary subtest of the Wechsler Adult Intelligence Scale (WAIS). No significant group differences in cognitive function were noted and, given the confounding role of the situational stress associated with exposure, the abnormalities noted could not be attributed to dioxin.

As one of the few epidemiological studies in humans to incorporate serum dioxin data into psychometric analyses, the National Institute for Occupational Safety and Health's study of chemical plant workers deserves special mention (23). This cross-sectional study of 281 workers in two industrial plants

investigated the association between exposure to chemicals (including dioxin) and symptoms of depression revealed by a battery of psychological screening tests (the Beck Depression Inventory and the depression subscale of the Symptom Checklist-90-Revised [SCL-90-R]). The mean serum dioxin level in the exposed cohort was 220 parts per trillion (ppt) versus 6 ppt in referents. By both scales, the prevalence of depression was comparable in each group. Of interest and consistent with numerous other reports, the self-perception of dioxin exposure was significantly associated with depressive symptoms, although the mean serum dioxin level in those thought to have been exposed (43 ppt) was significantly lower than that in the group reporting no such exposure (116 ppt).

The association between psychological symptoms and reported herbicide exposure during military service in Vietnam has been the subject of numerous studies. In one Veterans' Administration study of 153 veterans, a subgroup of 58 subjects reporting moderate to high herbicide exposure was compared to the remaining 95 patients reporting no or minimal exposure. After covariate adjustment, the self-reported exposed group had scores on the MMPI that indicated depression, poor morale, organic symptoms, family problems, and hypomania (24). Similar conclusions were reached in a more recent study of 7,924 United States Army veterans whose reported exposure to herbicides was a powerful predictor of a broad spectrum of negative mental and physical health outcomes (25).

Another large-scale study of 6,810 Vietnam veterans who belong to the American Legion found that, although perceived exposure to herbicides could not independently predict psychosocial outcomes, it was associated with such outcomes when combined with combat, indicating that a synergistic effect may have occurred (26).

Further evidence that service in Vietnam may be associated with psychological morbidity independent of exposure to herbicides is presented in the Vietnam Experience Study, conducted by the United States Centers for Disease Control and Prevention (27). This report, which included comprehensive psychological testing but did not include serum dioxin measurements, revealed an increased incidence of psychological dysfunction related to service in Vietnam, including depression (4.5 percent of Vietnam veterans versus 3.2 percent in non-Vietnam veterans), anxiety (4.9 percent versus 3.2 percent, respectively), and alcohol abuse or dependence (13.7 percent versus 9.2 percent, respectively).

Prior reports of the Air Force Health Study (AFHS) have revealed few statistically significant differences in the psychological indices between the Ranch Hand and Comparison cohorts (28–30). In the 1987 examinations, Ranch Hands demonstrated a greater level of depression, manifested more physical complaints (somatization), and felt more health-related anxiety than Comparisons (30).

12.1.2 Summary of Previous Analyses of the Air Force Health Study

12.1.2.1 1982 Baseline Study Summary Results

An extensive battery of psychological parameters was assessed on all participants during the 1982 baseline questionnaire and as part of the physical examination process. There were no questionnaire differences for past history of emotional or psychological illnesses between the Ranch Hand and Comparison groups. For the psychological indices of fatigue, anger, erosion of skills, anxiety, and severity of depression (as determined by a modification of the Diagnostic Interview Schedule), no group differences were detected among the college-educated Ranch Hands. For the high school-educated stratum, Ranch Hands demonstrated significantly more fatigue, anger, erosion of skills, and anxiety. An unadjusted analysis of reported depression showed significantly more depression in the Ranch Hands, as did the isolation index adjusted for educational level.

At the time of the physical examination, additional data were collected with the Cornell Index (CI) and the MMPI. The CNS functional testing was conducted by a modified Halstead-Reitan Battery (HRB) and intelligence was measured by the WAIS.

The CI showed a significant increase in psychophysiological symptoms in the high school-educated Ranch Hands. MMPI results in the high school-educated participants showed Ranch Hand mean values significantly increased in the scales of denial, hypochondria, masculinity-femininity, and mania-hypomania as contrasted to the college-educated participants. The social introversion scale was significantly decreased in the college-educated Ranch Hands. The effect of education was influential ($p<0.01$) in all scales of the MMPI. None of the self-reported data, including those from the in-home questionnaire, was adjusted for possible group differences in post-traumatic stress disorder (PTSD) or combat experience and intensity.

Performance testing by the HRB showed no neuropsychiatric impairment in the Ranch Hands in contrast to the results of the self-administered MMPI and the CI. The effect of education on the HRB testing was strong ($p<0.0001$). WAIS intelligence scores revealed group similarities in the full-scale and verbal and performance scales. As expected, the intelligence quotient (IQ) of college graduates was significantly higher than the IQ of high school graduates.

12.1.2.2 1985 Follow-up Study Summary Results

Two of the psychological tests (MMPI, HRB) conducted at the 1982 baseline examination were repeated at the first follow-up examination in 1985. An updated history of mental and emotional disorders and combat experience in Vietnam also was obtained on all participants. An indicator of PTSD was derived from a new MMPI subscale and was used for covariate adjustments of non-MMPI psychological data. The Cornell Medical Index (CMI) was substituted for the CI in the 1985 psychological assessment. Questionnaire data (verified by a medical records review) for the lifetime events of psychotic illness, alcohol dependence, anxiety, or other neuroses disclosed no significant differences between groups for these conditions.

The group distributions for the 14 MMPI variables, each stratified by the three occupational categories, were examined. Two of the 42 tests approached statistical significance (psychopathic deviate for enlisted flyers and mania/hypomania for officers). Ranch Hand enlisted flyers had a lower mean than Comparison enlisted flyers, and Ranch Hand officers had a higher mean than Comparison officers. The group distributions of the total CMI score were similarly contrasted, with separate analyses performed with stratification by the five covariates of age, race, occupation, education, and current alcohol drinking status. For one stratum of each of these covariates (born in or after 1942, non-Black, enlisted groundcrew, high school education, and current alcohol drinker), a significant difference in the distribution of the Ranch Hand and Comparison scores was found. In all cases for the CMI, the Ranch Hand mean was greater than the Comparison mean.

The unadjusted analyses showed a significant difference for the MMPI scales of denial ($p<0.001$) and masculinity-femininity ($p=0.017$), the total CMI ($p<0.001$), and the Section A-H area subscore ($p=0.003$). A marginally significant difference was observed for the MMPI scales of hysteria ($p=0.067$) and social introversion ($p=0.069$). Comparisons had a greater percentage of abnormal scores for the denial and masculinity-femininity scales, whereas Ranch Hands showed adverse findings for the total CMI, the Section A-H area subscore, hysteria, and social introversion.

The adjusted analyses were generally similar to the unadjusted analyses with respect to group differences. The MMPI scales of denial and masculinity-femininity were statistically significant in both the adjusted and unadjusted analyses, where Comparisons showed an adverse effect over Ranch Hands. The A-H

subscore of the CMI (suggesting diffuse medical problems) also was significant, where Ranch Hands had higher mean scores than Comparisons, suggesting that Ranch Hands had more illness. The M-R subscore of the CMI, a broad indicator of emotional health, was not statistically different between the two groups.

The HRB impairment index, a measure of CNS functional integrity, did not differ significantly between the Ranch Hand and Comparison groups. Strong covariates in the adjusted analysis were age, race, and education.

Because of alternate statistical models and slightly different psychological testing parameters, a direct contrast between the psychological results of the baseline and 1985 follow-up examinations was not always possible. Several broad patterns were observed: the discordance between distributional tests and results from traditional statistical models of the MMPI variables was noted with data from both examinations; there was a narrowing of group differences at the 1985 follow-up examination for most variables, either by a decrease in Ranch Hand reporting or by an increase in Comparison reporting; and as at the baseline examination, functional CNS testing, as measured by the HRB impairment index, showed no group differences and did not support an organic basis for differences in self-reported symptomatology. The longitudinal analysis of two MMPI scales—depression and denial—showed a significant reversal of depression seen at the baseline examination in the high school-educated Ranch Hands. The number of depression abnormalities decreased in Ranch Hands and increased in Comparisons.

The determination of PTSD in both Air Force cohorts by a relatively new MMPI scale showed a prevalence rate of less than 1 percent. This low rate was strongly influenced by characteristics of the study population (e.g., age, education, and military occupation).

In conclusion, significant test results were present in both groups or were noted in specific subgroups of a covariate. Educational level, age, and alcohol use showed strong effects on the psychological scales and scores in this psychological assessment. Tests of the CNS by the HRB demonstrated a similar prevalence of abnormality in both groups. Ranch Hands exhibited an increased mean A-H subscore of the CMI, suggesting they had more illness than Comparisons.

12.1.2.3 1987 Follow-up Study Summary Results

The psychological assessment was based on verified psychological disorders, reported sleep disorders, and two clinical psychological tests, the SCL-90-R and the Millon Clinical Multiaxial Inventory (MCMI). The verified data on lifetime psychological disorders showed no group differences for psychoses, drug dependence, and anxiety. Marginally more Ranch Hands than Comparisons had a verified history of alcohol dependence and other neuroses based on unadjusted analyses. The Ranch Hands reported experiencing great or disabling fatigue during the day and talking in their sleep more frequently than the Comparisons. No group differences were detected in the other 13 sleep disorder variables in the unadjusted analyses. Although no significant differences between the Ranch Hands and the Comparisons were found in the unadjusted analyses of the 12 SCL-90-R variables, the Ranch Hands had marginally more abnormalities than the Comparisons for depression, somatization, and an index of the general severity of symptoms. The results of the unadjusted analyses of the MCMI scores revealed that the Ranch Hands had significantly higher mean antisocial and paranoid scores than the Comparisons. Marginally significant differences were identified on the narcissistic and psychotic delusion scores, where the mean score of the Ranch Hands exceeded that of the Comparisons. After adjustment for the covariates, a significant increase in the Ranch Hand mean remained on the narcissistic score. The Comparisons had a significantly higher mean dependent score than the Ranch Hands.

12.1.2.4 Serum Dioxin Analysis of 1987 Follow-up Study Summary Results

In general, the results of the analyses of the verified psychological disorders, reported sleep disorders, and the SCL-90-R variables did not reveal significant associations with initial dioxin or current dioxin and time since tour of duty or find significant differences among the four current dioxin categories. In contrast, several of the analyses of the MCMI variables displayed significant results. There was a lack of consistency across similar variables included in the SCL-90-R, MCMI, and reported information. In conclusion, the body burden of dioxin did not appear to be related to psychological or psychophysiological disorders.

12.1.2.5 1992 Follow-up Study Summary Results

The psychological assessment was based on verified psychological disorders and the SCL-90-R. Differences in the SCL-90-R inventory variables were found between Ranch Hand and Comparison groups. Variables revealing significant or marginally significant differences in adjusted analyses were other neuroses, SCL-90-R anxiety, SCL-90-R hostility, SCL-90-R obsessive-compulsive behavior, SCL-90-R paranoid ideation, SCL-90-R somatization, and SCL-90-R global severity index. These differences were observed when combining participants across all occupations. All significant results showed a greater percentage of Ranch Hands than Comparisons that had a history of other neuroses or high (adverse) SCL-90-R scores. Many unadjusted analyses of the psychological endpoints showed associations with dioxin, but the results became nonsignificant when the analyses were adjusted for relevant covariates.

A marginally significant association between initial dioxin and the prevalence of high SCL-90-R psychoticism scores was observed in adjusted analyses, with the percentage of high SCL-90-R psychoticism scores increasing as initial dioxin increased. The same pattern and marginally significant association was observed with initial dioxin and high SCL-90-R global severity index scores. Most of the significant results in the adjusted analysis of the association between the psychological endpoints and categorized dioxin were from the contrasts of Ranch Hands in the background dioxin category with Comparisons. These differences between Ranch Hands in the background dioxin category and Comparisons were found in the analysis of the SCL-90-R obsessive-compulsive behavior, paranoid ideation, and somatization scores. The analysis also revealed that Ranch Hands in the background category had a larger percentage of high SCL-90-R scores than did Comparisons. The adjusted analysis of categorized dioxin also showed a significant increase in the percentage of Ranch Hands in the high dioxin category with a high SCL-90-R anxiety score over Comparisons. In the analyses of current dioxin, a significant inverse association between whole weight current dioxin, adjusted for total lipids, and a history of alcohol dependence was observed.

12.1.3 Parameters for the 1997 Psychological Assessment

12.1.3.1 Dependent Variables

Data collected through the SCL-90-R were used in the psychological assessment (31). In addition, psychological disorders, as verified through a medical records review, were used to supplement the psychological evaluation for the 1997 follow-up.

12.1.3.1.1 Medical Records Data

At the health interview during the 1997 examination, each participant was asked whether he had a mental or emotional disorder since the date of his last interview. Reported disorders for which treatment was obtained were subsequently verified by a review of medical records. Information on verified psychological disorders from the 1997 examination was combined with information on verified disorders

from the baseline and 1985, 1987, and 1992 follow-up examinations, and a series of dependent variables regarding verified history of psychological disorders was created. In particular, the verified histories of psychoses (International Classification of Diseases, 9th revision, Clinical Modification [ICD-9-CM] codes 290.0–298.9), alcohol dependence (ICD-9-CM codes 303.00–303.93), drug dependence (ICD-9-CM codes 304.00–304.93), anxiety (ICD-9-CM codes 300.00–300.09), and other neuroses (ICD-9-CM codes 300.10–302.9, 305.00–305.03, 305.20–309.9, and 311) were studied.

Participants with a verified pre-Southeast Asia (SEA) history of a psychological disorder were excluded from the analyses pertaining to that disorder. In addition, participants who tested positive for the human immunodeficiency virus (HIV) were excluded from all analyses of these variables.

12.1.3.1.2 Physical Examination Data

The SCL-90-R, used by the AFHS at the 1987 and 1992 follow-up examinations, was used again in the psychological assessment. The SCL-90-R is a multidimensional self-reported symptom inventory that measures symptomatic psychological distress in terms of nine primary symptom dimensions. The nine dimensions are anxiety, depression, hostility, interpersonal sensitivity, obsessive-compulsive behavior, paranoid ideation, phobic anxiety, psychoticism, and somatization. Each participant was asked to respond to 90 questions in terms of the following 5-point scale: 0=not at all, 1=a little bit, 2=moderately, 3=quite a bit, and 4=extremely. Responses were grouped into the nine primary symptom categories, and a raw score for a participant for a category was determined by adding the scores of the answered questions in that category and dividing by the number of answered questions in that category. The raw scores were then converted to T-scores (reference scores for a given population norm) for analysis.

The SCL-90-R also measures distress using three global indices: global severity index (GSI), positive symptom total (PST), and positive symptom distress index (PSDI). The GSI is defined as the sum of the scores of all answered questions divided by the number of answered questions on the entire test. This index combines information on the number of symptoms and the intensity of distress. The PST is the number of questions to which the participant responds positively (i.e., on the 5-point scale, responses 1, 2, 3, or 4). The PSDI is determined by adding the scores of all answered questions and dividing by the PST. This index describes the intensity of the positive symptoms. Each of these indices also was converted to a T-score.

The T-scores for the nine primary symptom dimensions and the three global indices were then classified as high or normal, where high was defined as a T-score of 63 or greater. All participants were included in the analyses of the nine primary symptom dimensions and the three global indices of distress, including those participants who responded "not at all" to all 90 questions. Participants who tested positive for HIV were excluded from the analysis of the SCL-90-R variables.

12.1.3.2 Covariates

Covariates examined in the adjusted statistical analyses of the psychological assessment included age, race, military occupation, education level (high school, college), current alcohol use (drinks/day), lifetime alcohol history (drink-years), current total household income, current employment (yes, no), current marital status (married, not married), and current parental status (currently having a child under the age of 18: yes, no). Age, race, and military occupation were determined from military records. Current total household income information was collected in the questionnaire in categories with $5,000 increments, between $5,000 and $100,000. The midpoint of each category was used as the current total household income, with $102,500 used for the $100,000 or more category. Educational level, current employment, current parental status, and current marital status were all based on self-reported information from the questionnaire.

Lifetime alcohol history was based on information from the 1997 questionnaire and combined with similar information gathered at the 1987 and 1992 follow-up examinations. Each participant was asked about his drinking patterns throughout his lifetime. When a participant's drinking patterns changed, he was asked to describe how his alcohol consumption differed and the duration of time that the drinking pattern lasted. The participant's average daily alcohol consumption was determined for each of the reported drinking pattern periods throughout his lifetime, and an estimate of the corresponding total number of drink-years was derived. One drink-year was the equivalent of drinking 1.5 ounces of an 80-proof alcoholic beverage, one 12-ounce beer, or one 5-ounce glass of wine per day for 1 year. Current alcohol use was based on the average number of drinks per day during the month prior to completing the questionnaire. These alcohol covariates were not used in adjusted analyses of alcohol dependence.

The covariates current total household income, current employment, current marital status, and current parental status were used in the analysis of dependent variables based on medical records data (psychoses, alcohol dependence, drug dependence, anxiety, and other neuroses). Although these dependent variables capture a history of the condition, and the covariates described above were based on the current status of a participant's life, the covariates were used as surrogate information to describe the participant's life experience. In addition, lifetime alcohol history was used as a covariate for these dependent variables, but current alcohol use was not used. Current alcohol use reflected a participant's alcohol use only in the month prior to the physical examination. The lifetime alcohol history covariate was used to investigate the cumulative lifetime effects of alcohol use.

12.1.4 Statistical Methods

Table 12-1 summarizes the statistical analyses performed for the 1997 psychological assessment. The first part of this table lists the dependent variables analyzed, data source, data form, cutpoints, covariates, and statistical analysis methods. The second part of this table provides a description of covariates examined. A covariate was used in its continuous form whenever possible for all adjusted analyses; if the covariate is inherently discrete (e.g., military occupation), or if a categorized form was needed to develop measures of association with the dependent variables, the covariate was categorized as shown in Table 12-1. Table 12-2 provides a summary of the number of participants with missing dependent variable and covariate data. In addition, the number of participants excluded because of medical conditions is given.

Table 12-1. Statistical Analysis for the Psychological Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
Psychoses	MR-V	D	Yes No	(1)	(a)	U:LR A:LR
Alcohol Dependence	MR-V	D	Yes No	(2)	(a)	U:LR A:LR
Drug Dependence	MR-V	D	Yes No	(1)	(a)	U:LR,CS A:LR
Anxiety	MR-V	D	Yes No	(1)	(a)	U:LR A:LR
Other Neuroses	MR-V	D	Yes No	(1)	(a)	U:LR A:LR

Table 12-1. Statistical Analysis for the Psychological Assessment (Continued)

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
SCL-90-R Anxiety	PE	D	High: T≥63 Normal: T<63	(3)	(b)	U:LR A:LR
SCL-90-R Depression	PE	D	High: T≥63 Normal: T<63	(3)	(b)	U:LR A:LR
SCL-90-R Hostility	PE	D	High: T≥63 Normal: T<63	(3)	(b)	U:LR A:LR
SCL-90-R Interpersonal Sensitivity	PE	D	High: T≥63 Normal: T<63	(3)	(b)	U:LR A:LR
SCL-90-R Obsessive-Compulsive Behavior	PE	D	High: T≥63 Normal: T<63	(3)	(b)	U:LR A:LR
SCL-90-R Paranoid Ideation	PE	D	High: T≥63 Normal: T<63	(3)	(b)	U:LR A:LR
SCL-90-R Phobic Anxiety	PE	D	High: T≥63 Normal: T<63	(3)	(b)	U:LR A:LR
SCL-90-R Psychoticism	PE	D	High: T≥63 Normal: T<63	(3)	(b)	U:LR A:LR
SCL-90-R Somatization	PE	D	High: T≥63 Normal: T<63	(3)	(b)	U:LR A:LR
SCL-90-R Global Severity Index (GSI)	PE	D	High: T≥63 Normal: T<63	(3)	(b)	U:LR A:LR
SCL-90-R Positive Symptom Total (PST)	PE	D	High: T≥63 Normal: T<63	(3)	(b)	U:LR A:LR
SCL-90-R Positive Symptom Distress Index (PSDI)	PE	D	High: T≥63 Normal: T<63	(3)	(b)	U:LR A:LR

[a]Covariates:
(1): age, race, military occupation, education, lifetime alcohol history, current total household income, current employment, current marital status, current parental status.
(2): age, race, military occupation, education, current total household income, current employment, current marital status, current parental status.
(3): age, race, military occupation, education, current alcohol use, lifetime alcohol history, current total household income, current employment, current marital status, current parental status.

[b]Exclusions:
(a): participants with a pre-SEA history of the disorder, participants testing positive for HIV.
(b): participants testing positive for HIV.

Covariates

Variable (Units)	Data Source	Data Form	Cutpoints
Age (years)	MIL	D/C	Born ≥1942 Born <1942
Race	MIL	D	Black Non-Black
Occupation	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew

Table 12-1. Statistical Analysis for the Psychological Assessment (Continued)

Variable (Units)	Data Source	Data Form	Cutpoints
Education	Q-SR	D	College High School
Current Alcohol Use (drinks/day)	Q-SR	D/C	0-1 >1–4 >4
Lifetime Alcohol History (drink-years)	Q-SR	D/C	0 >0–40 >40
Current Total Household Income (dollars)	Q-SR	D/C	≤$65,000 >$65,000
Current Employment	Q-SR	D	Yes No
Current Marital Status	Q-SR	D	Married Not Married
Current Parental Status	Q-SR	D	Child <18 years old No child <18 years old

Abbreviations

Data Source: MIL: Air Force military records
MR-V: Medical records (verified)
PE: 1997 Psychological examination
Q-SR: Health questionnaires (self-reported)

Data Form: D: Discrete analysis only
D/C: Appropriate form for analysis (either discrete or continuous)

Statistical Analysis: U: Unadjusted analysis
A: Adjusted analysis

Statistical Methods: CS: Chi-square contingency table analysis (continuity-adjusted)
LR: Logistic regression analysis

Table 12-2. Number of Participants Excluded or with Missing Data for the Psychological Assessment

Variable	Variable Use	Group: Ranch Hand	Group: Comparison	Dioxin (Ranch Hands Only): Initial	Dioxin (Ranch Hands Only): 1987	Categorized Dioxin: Ranch Hand	Categorized Dioxin: Comparison
SCL-90-R Categories and Indices	DEP	1	0	1	1	1	0
Education	COV	1	0	0	1	1	0
Current Alcohol Use	COV	1	0	0	1	1	0
Lifetime Alcohol History	COV	6	2	3	6	6	1

Table 12-2. Number of Participants Excluded or with Missing Data for the Psychological Assessment (Continued)

Variable	Variable Use	Group: Ranch Hand	Group: Comparison	Dioxin (Ranch Hands Only): Initial	Dioxin (Ranch Hands Only): 1987	Categorized Dioxin: Ranch Hand	Categorized Dioxin: Comparison
Current Total Household Income	COV	9	15	4	9	9	14
Current Employment	COV	1	0	0	1	1	0
Current Marital Status	COV	1	0	0	1	1	0
Current Parental Status	COV	1	0	0	1	1	0
Pre-SEA Alcohol Dependence	EXC	0	1	0	0	0	1
Pre-SEA Anxiety	EXC	4	3	2	4	4	3
Pre-SEA Other Neuroses	EXC	12	9	5	12	12	9
HIV Positive	EXC	3	2	3	3	3	2

Note: DEP = Dependent variable.
COV = Covariate.
EXC = Exclusion.
870 Ranch Hands and 1,251 Comparisons.
482 Ranch Hands for initial dioxin; 863 Ranch Hands for 1987 dioxin.
863 Ranch Hands and 1,213 Comparisons for categorized dioxin.

12.2 RESULTS

12.2.1 Dependent Variable-Covariate Associations

The psychological dependent variables were tested for significant association with each of the covariates used within the adjusted analyses. The results are presented in Appendix F, Table F-4. These associations are pairwise between the dependent variable and the covariate and are not adjusted for any other covariates. Participants with a verified pre-SEA history of a psychological disorder were excluded from the analyses pertaining to that disorder. In addition, participants who tested positive for HIV were excluded from all analyses. A brief summary of the pattern of dependent variable-covariate associations is contained in the following paragraphs. This brief description is followed by a more detailed description of significant covariate associations with each dependent variable.

The psychological dependent variables each displayed significant associations with several of the covariates. For each significant association with age, the greater percentage of high SCL-90-R scores was among the younger participants. Race was found marginally significant with only two of the dependent variables, drug dependence and SCL-90-R paranoid ideation. Each association displayed the greater percentage of high scores among the Black participants. Occupation showed a significant association with all dependent variables except drug dependence. Officers consistently displayed the lowest percentage of psychological problems. Associations with education generally were significant. Each association displayed the higher prevalence of a psychological disorder or the greater percentage of high SCL-90-R scores among participants with only a high school education.

Current alcohol use was significantly or marginally significantly associated with most of the psychology dependent variables. For each association, the largest percentage of high SCL-90-R scores was among the heaviest current drinkers (in terms of drinks per day), followed by the lightest current drinkers. The results were similar for lifetime alcohol history. Current total household income and current marital status were significantly associated with most of the psychological dependent variables. Each of these associations for both covariates displayed a greater percentage of abnormalities among participants with a

lower income or among unmarried participants. A significant association with current employment was found for alcohol dependence and SCL-90-R somatization. Unemployed participants had a greater percentage of alcohol dependence and high somatization scores than did employed participants. The current parental status covariate was significantly associated with alcohol dependence. A larger percentage of participants with no child less than 18 years old had a history of alcohol dependence than participants with a child less than 18 years old.

A significant association between a history of psychoses and occupation (p=0.032) was found. Enlisted flyers displayed the highest proportion of history of psychoses (5.0%). Psychoses was also significantly associated with current total household income (p=0.010) and current marital status (p=0.001). The prevalence of psychoses decreased as income rose and was increased among unmarried participants (7.8%).

A history of alcohol dependence was significantly associated with occupation (p=0.014). The highest percentage of participants with alcohol dependence was among enlisted flyers (8.9%), followed by enlisted groundcrew (7.9%) and officers (4.9%). Current total household income also displayed a significant association with alcohol dependence (p=0.001). Participants with lower incomes were dependent on alcohol more often than those participants with higher incomes (8.8% vs. 5.0%). In addition, alcohol dependence was significantly associated with current employment (p=0.039), current marital status (p=0.001), and current parental status (p=0.009). The higher prevalence of alcohol dependence history was among those participants not currently employed (8.5%), not currently married (14.4%), or those without a child under the age of 18 (7.5%).

Current marital status was the only covariate found significantly associated with a history of drug dependence (p=0.008). The higher percentage of drug dependence was among participants who were currently unmarried (1.1%).

A history of anxiety showed significant associations with occupation (p=0.001), education (p=0.001), current total household income (p=0.001), and current marital status (p=0.001). Enlisted groundcrew showed the highest percentage of anxiety (33.9%), followed by enlisted flyers (30.9%) and officers (17.3%). Participants with only a high school education, in the lower income category, or who were not married had the higher percentages of anxiety (31.3%, 32.8%, and 34.0%, respectively).

Tests of association between covariates and a history of other neuroses revealed several significant results. The association with occupation (p=0.001) showed that enlisted flyers had the highest proportion of other neuroses (61.4%), followed by enlisted groundcrew (60.1%) and officers (43.7%). Education also displayed a significant association with other neuroses (p=0.001). Participants with only a high school education displayed the higher percentage of other neuroses (60.9%). The significant lifetime alcohol history association (p=0.001) showed 62.8 percent of the heaviest drinkers (in terms of drink-years) with other neuroses, followed by 50.9 percent of participants who did not drink, and 50.2 percent in the moderate lifetime drinking category. The association with current total household income (p=0.001) showed that the percentage of participants with other neuroses decreased as the income level increased. The association with current marital status found 62.9 percent of unmarried participants with history of other neuroses, compared to 51.9 percent of those married (p=0.001).

The SCL-90-R anxiety scores were significantly associated with occupation (p=0.001), education, (p=0.001), lifetime alcohol history (p=0.009), current total household income (p=0.001), and current marital status (p=0.028). The enlisted groundcrew stratum displayed the largest percentage of participants with a high SCL-90-R anxiety score (14.3%), followed by enlisted flyers (13.4%) and officers (5.0%). High SCL-90-R anxiety scores were greater among high school-educated participants

(14.1%) compared to those who were college-educated (7.5%). High anxiety scores were most prevalent in the heaviest lifetime drinkers (13.7%), followed by non-drinkers (11.0%) and moderate lifetime drinkers (9.1%). Participants in the lower income category and those not married displayed the greater percentages of high SCL-90-R anxiety scores (14.5% and 13.8%, respectively).

The significant covariate associations with the SCL-90-R depression score were found with age (p=0.040), occupation (p=0.001), education (p=0.001), current alcohol use (p=0.023), lifetime alcohol use (p=0.001), current total household income (p=0.001), and current marital status (p=0.002). High depression scores were more prevalent among younger participants (16.8%) and greatest among the enlisted groundcrew (19.3%). High school-educated participants displayed more high depression scores (19.4%) than college-educated participants (11.2%). Participants currently drinking the most had the largest percentage of high depression scores (28.0%). Similarly, participants with a lifetime history of drinking the most had largest percentage of high SCL-90-R depression scores (19.4%). The percentage of high SCL-90-R depression scores decreased as income level increased. The significant association with current marital status showed more high depression scores among unmarried participants (20.3%).

SCL-90-R hostility scores were significantly associated with age (p=0.038), occupation (p=0.001), education (p=0.001), current alcohol use (p=0.024), lifetime alcohol use (p=0.004), and current total household income (p=0.001). The prevalence of high SCL-90-R hostility scores decreased as age increased and was greatest for enlisted groundcrew (11.2%). High hostility scores were more prevalent among high school-educated participants (11.3%) than among college-educated participants (5.4%). Analysis of current alcohol use showed that the heaviest drinkers had the largest prevalence of high hostility scores (18.0%). The percentage of high hostility scores increased as the number of drink-years increased within the examination of lifetime alcohol history (3.4%, 7.4%, and 10.9% for non-drinkers, moderate drinkers, and heavy drinkers, respectively). The association with current total household income showed the greater percentage of high hostility scores among participants in the lower income category (10.6%).

Association tests between the SCL-90-R interpersonal sensitivity scores and age, occupation, education, current total household income, and current marital status were each significant (p=0.020, p=0.001, p=0.001, p=0.001, and p=0.023, respectively). Of the younger participants, 17.3 percent had high interpersonal sensitivity scores, compared to 13.6 percent for the older participants. The percentage of high scores was largest for enlisted groundcrew and enlisted flyers (20.4% and 19.0%, respectively). Participants with at most a high school education had almost twice the percentage of high SCL-90-R interpersonal sensitivity scores than college-educated participants (20.4% vs. 10.8%). Examination of current total household income and current marital status showed the greater percentages of high interpersonal sensitivity scores among participants in the lower income category (20.0%) and among those who were not married (19.2%).

SCL-90-R obsessive-compulsive behavior scores were significantly associated with occupation (p=0.001), education (p=0.001), lifetime alcohol history (p=0.002), and current total household income (p=0.001). Enlisted flyers displayed the greatest prevalence of high obsessive-compulsive scores (20.5%). Participants with at most a high school education had the greater percentage of high scores (19.7%), compared to college-educated participants (11.8%). Participants who were the heaviest lifetime drinkers displayed the largest proportion of high obsessive-compulsive behavior scores (19.8%). The association with current total household income showed the larger percentage of high SCL-90-R obsessive-compulsive scores among participants with lower incomes (20.8%), compared to 9.8 percent for participants with higher incomes.

Age, occupation, education, current total household income, and current marital status were each significantly associated with the SCL-90-R paranoid ideation (p=0.001, p=0.001, p=0.001, p=0.001, and p=0.002, respectively). Younger participants had a greater prevalence of high paranoid ideation scores (9.0%) than older participants (5.2%). The proportion of high paranoid ideation scores was largest for enlisted groundcrew (10.4%). High school-educated participants exhibited the larger proportion of high paranoid ideation scores (9.7%), as did participants with lower incomes (9.7%) and unmarried participants (10.8%).

Significant covariate associations with SCL-90-R phobic anxiety and SCL-90-R psychoticism were similar and included age (p=0.005 and p=0.025, respectively), occupation (p=0.001 for each), education (p=0.001 for each), lifetime alcohol history (p=0.014 and p=0.004, respectively), and current total household income (p=0.001 for each). Current marital status was also significantly associated with psychoticism (p=0.001). The percentage of high scores for both variables was higher among younger participants (12.4% and 15.6%, respectively) and highest among enlisted groundcrew (14.4% and 18.3%, respectively). High school-educated participants displayed the greater prevalence of high scores for both variables (14.5% and 17.1%, respectively). In addition, percentages of high scores increased for each variable as lifetime drinking increased. Participants with lower incomes displayed the greater proportion of high scores for each variable (14.1% and 18.1%, respectively). The percentage of high SCL-90-R psychoticism scores was increased among unmarried participants (19.2%).

Covariate association tests with SCL-90-R somatization were significant for occupation (p=0.001), education (p=0.001), current alcohol use (p=0.037), current total household income (p=0.001), and current employment (p=0.020). The percentage of high SCL-90-R somatization scores was greatest among enlisted flyers (25.2%), followed by enlisted groundcrew (21.0%) and officers (7.3%). Participants with at most a high school education displayed the greater proportion of high somatization scores (22.3%) compared to college-educated participants (11.2%). The prevalence of high somatization scores was greatest for the heaviest current drinkers (20.0%) and smallest for moderate drinkers (11.9%). Examination of current total household income and current employment revealed a greater proportion of high somatization scores among the lower income earners (21.8%) and among unemployed participants (18.9%).

Association tests with the SCL-90-R GSI were significant for age (p=0.048), occupation (p=0.001), education (p=0.001), current alcohol use (p=0.017), lifetime alcohol use (p=0.001), current total household income (p=0.001), and current marital status (p=0.016). Younger participants displayed the greater percentage of high GSI scores (16.6%), as did enlisted groundcrew (20.1%). The percentage of high GSI scores was also larger among participants with at most a high school education (19.2%) compared to college-educated participants (11.1%). The greatest percentage of high GSI scores was among the heaviest current drinkers (28.0%), as well as among the heaviest lifetime drinkers (19.5%). High GSI scores were more prevalent among participants in the lower income bracket (19.9%) and among the unmarried participants (19.0%).

Occupation, education, lifetime alcohol use, and current total household income each displayed significant associations with the SCL-90-R PST scores (p=0.001, p=0.001, p=0.002, and p=0.001, respectively). The percentages of high PST scores for enlisted groundcrew, enlisted flyers, and officers were 20.9 percent, 20.2 percent, and 8.5 percent, respectively. High school-educated participants displayed a larger percentage of high scores (20.8%) than did college-educated participants (11.7%). The prevalence of high SCL-90-R PST scores was greatest among the heaviest lifetime drinkers (20.3%). Participants in the lower income category showed the larger percentage of high SCL-90-R PST scores (21.0%).

The SCL-90-R PSDI displayed significant covariate associations with occupation (p=0.001), education (p=0.001), current alcohol use (p=0.030), and current total household income (p=0.012). High PSDI

scores were more prevalent among enlisted groundcrew and enlisted flyers (9.5% for each) than among officers (3.7%). Participants with at most a high school education displayed the greater percentage of high SCL-90-R PSDI scores (9.5%), and the heaviest current drinkers showed the highest percentage (12.0%). The prevalence of high SCL-90-R PSDI scores was greatest for participants with lower incomes (8.7%).

12.2.2 Exposure Analysis

The following section presents results of the statistical analyses of the dependent variables shown in Table 12-1. Dependent variables were derived from a medical records review and verification of self-reported psychological conditions and the psychological examination portion of the 1997 follow-up examination.

Four models were examined for each dependent variable given in Table 12-1. The analyses of these models are presented below. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7, respectively. These analyses were performed both unadjusted and adjusted for relevant covariates. Model 1 examined the relation between the dependent variable and group (i.e., Ranch Hand or Comparison). In this model, exposure was defined as "yes" for Ranch Hands and "no" for Comparisons without regard to the magnitude of the exposure. As an attempt to quantify exposure, three contrasts of Ranch Hands and Comparisons were performed along with the overall Ranch Hand versus Comparison contrast. These three contrasts compared Ranch Hands and Comparisons within each occupational category (i.e., officers, enlisted flyers, and enlisted groundcrew). As described in previous reports and Table 2-8, the average levels of exposure to dioxin were highest for enlisted groundcrew, followed by enlisted flyers, then officers.

Model 2 explored the relation between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt. If a participant did not have a 1987 dioxin level, the 1992 level was used to estimate the initial dioxin level. If a participant did not have a 1987 or a 1992 dioxin level, the 1997 level was used to estimate the initial dioxin level. A statistical adjustment for the percentage of body fat at the time of the participant's blood measurement of dioxin was included in this model to account for body-fat-related differences in elimination rate (32).

Model 3 divided the Ranch Hands examined in Model 2 into two categories based on their initial dioxin measures. These two categories are referred to as "low Ranch Hand" and "high Ranch Hand." Two additional categories, Ranch Hands with 1987 serum dioxin levels at or below 10 ppt and Comparisons with 1987 serum dioxin levels at or below 10 ppt, were formed and included in the model. Ranch Hands with 1987 serum dioxin levels at or below 10 ppt are referred to as the "background Ranch Hand" category. Dioxin levels in 1992 were used if the 1987 level was not available, and dioxin levels in 1997 were used if the 1987 and 1992 levels were not available. These four categories—Comparisons, background Ranch Hands, low Ranch Hands, and high Ranch Hands—were used in Model 3 analyses. The relation between the dependent variable in each of the three Ranch Hand categories and the dependent variable in the Comparison category was examined. A fourth contrast, exploring the relation of the dependent variable in the combined low and high Ranch Hand categories relative to Comparisons, also was conducted. This combination is referred to in the tables as the "low plus high Ranch Hand" category. As in Model 2, a statistical adjustment for the percentage of body fat at the time of the participant's blood measurement of dioxin was included in this model.

Model 4 examined the relation between the dependent variable and 1987 lipid-adjusted dioxin levels in all Ranch Hands with a dioxin measurement. If a participant did not have a 1987 dioxin measurement, the 1992 measurement was used to determine the dioxin level. If a participant did not have a 1987 or a 1992 dioxin measurement, the 1997 measurement was used to determine the dioxin level.

12.2.2.1 *Medical Records Variables*

12.2.2.1.1 *Psychoses*

All results from the analyses of a history of psychoses (Models 1 through 4) were nonsignificant, both unadjusted and adjusted for covariates (Table 12-3(a–h): $p \geq 0.23$ for each analysis).

Table 12-3. Analysis of Psychoses

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***867***	***34 (3.9)***	***1.02 (0.65,1.60)***	***0.927***
	Comparison	***1,249***	***48 (3.8)***		
Officer	Ranch Hand	341	9 (2.6)	1.09 (0.45,2.61)	0.853
	Comparison	493	12 (2.4)		
Enlisted Flyer	Ranch Hand	151	10 (6.6)	1.82 (0.68,4.91)	0.235
	Comparison	187	7 (3.7)		
Enlisted Groundcrew	Ranch Hand	375	15 (4.0)	0.78 (0.41,1.47)	0.435
	Comparison	569	29 (5.1)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.03 (0.65,1.63)***	***0.905***
Officer	1.12 (0.47,2.71)	0.796
Enlisted Flyer	1.85 (0.68,5.04)	0.230
Enlisted Groundcrew	0.76 (0.40,1.47)	0.423

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	10 (6.3)	0.90 (0.65,1.24)	0.501
Medium	162	7 (4.3)		
High	157	7 (4.5)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
472	0.82 (0.55,1.23)	0.338

[a] Relative risk for a twofold increase in initial dioxin.

Table 12-3. Analysis of Psychoses (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	47 (3.9)		
Background RH	381	10 (2.6)	0.71 (0.35,1.43)	0.339
Low RH	239	12 (5.0)	1.29 (0.67,2.47)	0.447
High RH	240	12 (5.0)	1.23 (0.64,2.36)	0.535
Low plus High RH	479	24 (5.0)	1.26 (0.76,2.09)	0.373

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,196		
Background RH	374	0.85 (0.41,1.73)	0.648
Low RH	236	1.42 (0.73,2.77)	0.297
High RH	236	0.90 (0.45,1.80)	0.759
Low plus High RH	472	1.13 (0.67,1.91)	0.647

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	9 (3.1)	1.11 (0.89,1.39)	0.368
Medium	287	12 (4.2)		
High	285	13 (4.6)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 12-3. Analysis of Psychoses (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
846	1.08 (0.84,1.40)	0.550

[a] Relative risk for a twofold increase in 1987 dioxin.

12.2.2.1.2 Alcohol Dependence

All unadjusted and adjusted results from the analysis of alcohol dependence were nonsignificant for Models 1 through 4 (Table 12-4(a–h): p>0.30 for each analysis).

Table 12-4. Analysis of Alcohol Dependence

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***867***	***62 (7.2)***	***1.08 (0.77,1.52)***	***0.655***
	Comparison	***1,248***	***83 (6.7)***		
Officer	Ranch Hand	341	15 (4.4)	0.83 (0.43,1.58)	0.566
	Comparison	493	26 (5.3)		
Enlisted Flyer	Ranch Hand	151	14 (9.3)	1.09 (0.52,2.32)	0.818
	Comparison	187	16 (8.6)		
Enlisted Groundcrew	Ranch Hand	375	33 (8.8)	1.24 (0.77,2.00)	0.377
	Comparison	568	41 (7.2)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.04 (0.74,1.48)***	***0.816***
Officer	0.82 (0.43,1.58)	0.557
Enlisted Flyer	0.94 (0.43,2.04)	0.871
Enlisted Groundcrew	1.25 (0.76,2.03)	0.377

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	14 (8.8)	1.04 (0.81,1.34)	0.747
Medium	162	10 (6.2)		
High	157	14 (8.9)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 12-4. Analysis of Alcohol Dependence (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
475	1.04 (0.77,1.42)	0.790

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for parental status because of the sparse number of participants with alcohol dependence.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,210	80 (6.6)		
Background RH	381	24 (6.3)	0.93 (0.58,1.50)	0.767
Low RH	239	18 (7.5)	1.16 (0.68,1.97)	0.594
High RH	240	20 (8.3)	1.31 (0.78,2.18)	0.307
Low plus High RH	479	38 (7.9)	1.23 (0.82,1.84)	0.316

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,196		
Background RH	376	1.04 (0.63,1.69)	0.888
Low RH	237	1.11 (0.64,1.91)	0.714
High RH	238	1.01 (0.58,1.73)	0.985
Low plus High RH	475	1.05 (0.69,1.60)	0.802

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 12-4. Analysis of Alcohol Dependence (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	16 (5.6)	1.07 (0.90,1.28)	0.420
Medium	287	24 (8.4)		
High	285	22 (7.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
851	0.99 (0.82,1.20)	0.898

[a] Relative risk for a twofold increase in 1987 dioxin.

12.2.2.1.3 Drug Dependence

Only a small percentage of participants had a verified drug dependence; consequently, analysis of drug dependence was limited. All analyses performed for Models 1, 3, and 4 indicated no differences among Ranch Hands and Comparisons and no association between dioxin levels and a history of drug dependence (Table 12-5(a–b,e–h): p>0.15 for all analyses). No Ranch Hands with extrapolated initial dioxin levels (Model 2) had a drug dependence.

Table 12-5. Analysis of Drug Dependence

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***867***	***2 (0.2)***	***0.72 (0.13,3.94)***	***0.700***
	Comparison	***1,249***	***4 (0.3)***		
Officer	Ranch Hand	341	0 (0.0)	--	0.999[a]
	Comparison	493	1 (0.2)		
Enlisted Flyer	Ranch Hand	151	0 (0.0)	--	--
	Comparison	187	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	375	2 (0.5)	1.01 (0.17,6.08)	0.990
	Comparison	569	3 (0.5)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with drug dependence.
--: Results not presented because of the sparse number of participants with drug dependence.

Table 12-5. Analysis of Drug Dependence (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.58 (0.09,3.74)***	***0.553***
Officer	--	--
Enlisted Flyer	--	--
Enlisted Groundcrew	0.78 (0.11,5.56)	0.802

--: Results not presented because of the sparse number of participants with drug dependence.

Note: Results are not adjusted for current employment because of the sparse number of participants with drug dependence; in addition, results for all occupational categories combined not adjusted for occupation.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)	p-Value
Low	160	0 (0.0)	--	--
Medium	162	0 (0.0)		
High	157	0 (0.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

--: Results not presented because of the sparse number of participants with drug dependence.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)	p-Value
--	--	--

--: Results not presented because of the sparse number of participants with drug dependence.

Table 12-5. Analysis of Drug Dependence (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	**n**	**Number (%) Yes**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,211	4 (0.3)		
Background RH	381	2 (0.5)	1.32 (0.24,7.34)	0.749
Low RH	239	0 (0.0)	--	0.830[c]
High RH	240	0 (0.0)	--	0.828[c]
Low plus High RH	479	0 (0.0)	--	0.481[c]

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with drug dependence.
--: Results not presented because of the sparse number of participants with drug dependence.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Comparison	1,196		
Background RH	374	1.37 (0.19,9.67)	0.755
Low RH	236	--	--
High RH	236	--	--
Low plus High RH	472	--	--

[a] Relative risk and confidence interval relative to Comparisons.
--: Results not presented because of the sparse number of participants with drug dependence.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for current employment or occupation because of the sparse number of participants with drug dependence.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**	
1987 Dioxin	**n**	**Number (%) Yes**	**Estimated Relative Risk (95% C.I.)[a]**	**p-Value**
Low	288	2 (0.7)	0.46 (0.16,1.34)	0.155
Medium	287	0 (0.0)		
High	285	0 (0.0)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 12-5. Analysis of Drug Dependence (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
846	0.45 (0.10,2.11)	0.226

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race, occupation, current employment, current marital status, and current parental status because of the sparse number of participants with drug dependence.

12.2.2.1.4 Anxiety

The unadjusted and adjusted analysis results for a history of anxiety were nonsignificant for both Models 1 and 2 (Table 12-6(a–d): p>0.30 for each analysis).

Table 12-6. Analysis of Anxiety

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***863***	***232 (26.9)***	***1.00 (0.83,1.22)***	***0.969***
	Comparison	***1,246***	***334 (26.8)***		
Officer	Ranch Hand	340	56 (16.5)	0.91 (0.63,1.31)	0.605
	Comparison	493	88 (17.9)		
Enlisted Flyer	Ranch Hand	150	48 (32.0)	1.10 (0.69,1.75)	0.685
	Comparison	187	56 (30.0)		
Enlisted Groundcrew	Ranch Hand	373	128 (34.3)	1.03 (0.78,1.36)	0.813
	Comparison	566	190 (33.6)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.00 (0.82,1.23)***	***0.979***
Officer	0.93 (0.64,1.35)	0.709
Enlisted Flyer	1.01 (0.63,1.63)	0.953
Enlisted Groundcrew	1.04 (0.79,1.38)	0.776

Table 12-6. Analysis of Anxiety (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	159	41 (25.8)	1.07 (0.92,1.24)	0.360
Medium	162	55 (34.0)		
High	156	47 (30.1)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
470	0.91 (0.76,1.09)	0.302

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,208	328 (27.2)		
Background RH	379	86 (22.7)	0.78 (0.60,1.03)	0.083
Low RH	238	70 (29.4)	1.12 (0.82,1.52)	0.473
High RH	239	73 (30.5)	1.18 (0.87,1.60)	0.279
Low plus High RH	477	143 (30.0)	1.15 (0.91,1.45)	0.240

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 12-6. Analysis of Anxiety (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,194		
Background RH	372	0.98 (0.74,1.31)	0.902
Low RH	235	1.17 (0.85,1.60)	0.343
High RH	235	0.82 (0.59,1.13)	0.225
Low plus High RH	470	0.98 (0.77,1.25)	0.857

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	286	62 (21.7)	1.14 (1.03,1.26)	0.011
Medium	286	76 (26.6)		
High	284	91 (32.0)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
842	0.95 (0.84,1.07)	0.368

[a] Relative risk for a twofold increase in 1987 dioxin.

The Model 3 unadjusted analysis revealed marginally significantly more Comparisons than Ranch Hands with anxiety (Table 12-6(e): p=0.083, Est. RR=0.78). After adjustment for covariates, the difference was nonsignificant (Table 12-6(f): p=0.902). All other Model 3 contrasts were nonsignificant (Table 12-6(e,f): p>0.22).

A significant positive association between 1987 dioxin levels and anxiety was found from the unadjusted Model 4 analysis (Table 12-6(g): p=0.011, Est. RR=1.14). Similar to Model 3 results, the association was nonsignificant after covariate adjustment (Table 12-6(h): p=0.368).

12.2.2.1.5 Other Neuroses

The Model 1 unadjusted analysis of a history of other neuroses showed a marginally significant difference between Ranch Hands and Comparisons within the officer stratum (Table 12-7(a): p=0.099, Est. RR=0.79). This difference became nonsignificant after adjustment for covariates (Table 12-7(b): p=0.127, Adj. RR=0.80). A significant difference within the enlisted groundcrew stratum was seen for both the unadjusted and adjusted contrasts (Table 12-7(a,b): p=0.021, Est. RR=1.38; p=0.011, Adj. RR=1.44, respectively). For Ranch Hand enlisted groundcrew, 64.7 percent had other neuroses, as compared to 57.1 percent of Comparison enlisted groundcrew. All other Model 1 contrasts were nonsignificant (Table 12-7(a,b): p>0.43).

Table 12-7. Analysis of Other Neuroses

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***855***	***467 (54.6)***	***1.06 (0.89,1.26)***	***0.529***
	Comparison	***1,240***	***660 (53.2)***		
Officer	Ranch Hand	338	136 (40.2)	0.79 (0.60,1.05)	0.099
	Comparison	491	226 (46.0)		
Enlisted Flyer	Ranch Hand	149	93 (62.4)	1.08 (0.69,1.69)	0.726
	Comparison	185	112 (60.5)		
Enlisted Groundcrew	Ranch Hand	368	238 (64.7)	1.38 (1.05,1.80)	0.021
	Comparison	564	322 (57.1)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.08 (0.90,1.29)***	***0.434***
Officer	0.80 (0.60,1.07)	0.127
Enlisted Flyer	1.04 (0.66,1.65)	0.857
Enlisted Groundcrew	1.44 (1.09,1.91)	0.011

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	158	90 (57.0)	1.02 (0.89,1.18)	0.743
Medium	161	104 (64.6)		
High	155	98 (63.2)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 12-7. Analysis of Other Neuroses (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
467	0.88 (0.74,1.05)	0.164

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,202	637 (53.0)		
Background RH	374	170 (45.5)	0.75 (0.60,0.95)	0.018
Low RH	237	143 (60.3)	1.34 (1.01,1.79)	0.041
High RH	237	149 (62.9)	1.48 (1.11,1.97)	0.008
Low plus High RH	474	292 (61.6)	1.41 (1.13,1.75)	0.002

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,187		
Background RH	367	0.89 (0.69,1.14)	0.368
Low RH	234	1.37 (1.02,1.84)	0.036
High RH	233	1.18 (0.87,1.61)	0.286
Low plus High RH	467	1.27 (1.01,1.60)	0.038

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 12-7. Analysis of Other Neuroses (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	282	127 (45.0)	1.20 (1.09,1.32)	<0.001
Medium	284	152 (53.5)		
High	282	183 (64.9)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
834	1.02 (0.91,1.14)	0.763

[a] Relative risk for a twofold increase in 1987 dioxin.

Model 2 analyses of other neuroses were nonsignificant, both unadjusted and adjusted for covariates (Table 12-7(c,d): p>0.16 for each analysis).

Each contrast of Ranch Hands with Comparisons in the unadjusted Model 3 analysis of other neuroses was significant (Table 12-7(e): p=0.018, Est. RR=0.75, for the Ranch Hand background dioxin category contrast; p=0.041, Est. RR=1.34, for the Ranch Hand low dioxin category contrast; p=0.008, Est. RR=1.48, for the Ranch Hand high dioxin category contrast; p=0.002, Est. RR=1.41, for the contrast of Ranch Hands in the combined low and high dioxin categories with Comparisons). Except for Ranch Hands in the background category, a higher proportion of Ranch Hands had other neuroses than did Comparisons. Results remained significant in the adjusted analysis of Ranch Hands in the low dioxin category (Table 12-7(f): p=0.036, Adj. RR=1.37) and the adjusted analysis of Ranch Hands in the combined low and high dioxin categories (Table 12-7(f): p=0.038, Adj. RR=1.27). The remaining adjusted analyses were nonsignificant (Table 12-7(f): p>0.28).

The Model 4 unadjusted analysis of other neuroses revealed a significant positive association between 1987 dioxin levels and other neuroses (Table 12-7(g): p<0.001, Est. RR=1.20). After accounting for covariates, the association was nonsignificant (Table 12-7(h): p=0.763).

12.2.2.2 Psychological Examination Variables

The 12 variables contained in this section are derived from the SCL-90-R. These 12 variables consist of nine primary symptom disease categories and three global indices of distress. A short description, which has been taken from the SCL-90-R reference manual (31), of each of the primary symptom disease categories and global indices of distress is given before the description of the results of the statistical analyses. The function of each of these global measures of the SCL-90-R, the GSI, the PSDI, and the PST, is to communicate in a single score the level or depth of the individual's psychopathology.

Seven items are a part of the SCL-90-R, which are not subsumed under any of the primary symptom dimensions; these symptoms actually "load" on several of the dimensions but are not unique to any of them. These seven items are having a poor appetite, overeating, having trouble falling asleep, awakening in the early morning, experiencing restless or disturbed sleep, thinking of death or dying, and feeling guilty. While in this sense they violate one of the statistical criteria for inclusion in the test, they are a part of the item set because they are clinically important. These items contribute to the global scores on the SCL-90-R and are intended to be used configurally. Thus, a high depression score with "early morning awakening" and "poor appetite" may mean something quite different from a similar score with these symptoms absent. By the same token, the presence of conscious "feelings of guilt" is an important clinical indicator that communicates important information to the clinician. The additional items are not scored collectively as a dimension but are summed into the global scores.

12.2.2.2.1 SCL-90-R Anxiety

The anxiety dimension is composed of a set of symptoms and signs that are associated clinically with high levels of manifest anxiety. General signs such as nervousness, tension, and trembling are included in the definition, as are panic attacks and feelings of terror. Cognitive components involving feelings of apprehension and dread, and some of the somatic correlates of anxiety, also are included as dimensional components. The symptoms comprising the anxiety dimension are experiencing nervousness or shakiness inside, trembling, being suddenly scared for no reason, feeling fearful, experiencing heart pounding or racing, feeling tense and keyed up, having spells of terror and panic, feeling so restless you couldn't sit still, feeling that something bad is going to happen, and experiencing frightening thoughts and images.

The Model 1 unadjusted analysis of SCL-90-R anxiety revealed no significant differences between Ranch Hands and Comparisons when examined across all occupations or within each occupational stratum (Table 12-8(a): p>0.10 for each contrast). When covariates were entered into the Model 1 analysis, a marginally significant difference was found for enlisted flyers (Table 12-8(b): p=0.073, Adj. RR=0.53). High SCL-90-R anxiety scores were more prevalent among Comparison enlisted flyers than Ranch Hand enlisted flyers (16.0% vs. 10.0%).

Table 12-8. Analysis of SCL-90-R Anxiety

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***82 (9.5)***	***0.83 (0.62,1.10)***	***0.197***
	Comparison	***1,249***	***140 (11.2)***		
Officer	Ranch Hand	341	14 (4.1)	0.71 (0.37,1.37)	0.309
	Comparison	493	28 (5.7)		
Enlisted Flyer	Ranch Hand	150	15 (10.0)	0.58 (0.30,1.13)	0.108
	Comparison	187	30 (16.0)		
Enlisted Groundcrew	Ranch Hand	375	53 (14.1)	0.98 (0.67,1.42)	0.905
	Comparison	569	82 (14.4)		

Table 12-8. Analysis of SCL-90-R Anxiety (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.85 (0.63,1.14)***	***0.267***
Officer	0.75 (0.39,1.46)	0.400
Enlisted Flyer	0.53 (0.27,1.06)	0.073
Enlisted Groundcrew	1.02 (0.70,1.50)	0.904

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	19 (11.9)	0.98 (0.79,1.21)	0.847
Medium	161	19 (11.8)		
High	157	17 (10.8)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
471	0.73 (0.57,0.95)	0.016

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	133 (11.0)		
Background RH	381	27 (7.1)	0.65 (0.42,1.00)	0.051
Low RH	239	26 (10.9)	0.98 (0.63,1.53)	0.919
High RH	239	29 (12.1)	1.07 (0.70,1.65)	0.756
Low plus High RH	478	55 (11.5)	1.02 (0.73,1.43)	0.895

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 12-8. Analysis of SCL-90-R Anxiety (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,196		
Background RH	374	0.86 (0.55,1.35)	0.506
Low RH	236	1.09 (0.69,1.73)	0.717
High RH	235	0.76 (0.48,1.20)	0.237
Low plus High RH	471	0.91 (0.64,1.29)	0.595

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	19 (6.6)	1.15 (0.99,1.34)	0.065
Medium	287	30 (10.5)		
High	284	33 (11.6)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
845	0.96 (0.81,1.13)	0.619

[a] Relative risk for a twofold increase in 1987 dioxin.

Similar to Model 1, the result from the Model 2 unadjusted analysis of SCL-90-R anxiety was nonsignificant (Table 12-8(c): p=0.847). The adjusted analysis revealed a significant association between initial dioxin and the prevalence of high SCL-90-R anxiety scores (Table 12-8(d): p=0.016, Adj. RR=0.73). As initial dioxin increased, the prevalence of high SCL-90-R anxiety scores decreased.

The unadjusted Model 3 analysis revealed a marginally significant difference in the prevalence of high SCL-90-R anxiety scores among Ranch Hands in the background category (7.1%) and Comparisons (11.0%) (Table 12-8(e): p=0.051, Est. RR=0.65). Results were nonsignificant after adjustment for covariates (Table 12-8(f): p=0.506). Other Model 3 contrasts were nonsignificant (Table 12-8(e,f): p>0.23 for each contrast).

The unadjusted analysis of Model 4 revealed a marginally significant positive association between the 1987 dioxin levels and the prevalence of high SCL-90-R anxiety scores (Table 12-8(g): p=0.065, Est. RR=1.15). The results were nonsignificant after covariate adjustment (Table 12-8(h): p=0.619).

12.2.2.2.2 SCL-90-R Depression

The symptoms of the depression dimension reflect a broad range of the manifestations of clinical depression. Symptoms of dysphoric mood and affect are represented, as are signs of withdrawal of life interest, lack of motivation, and loss of vital energy. In addition, feelings of hopelessness, thoughts of suicide, and other cognitive and somatic correlates of depression are included. The symptoms comprising the depression dimension are losing sexual interest or pleasure, feeling low in energy or slowed down, thinking of ending your life, crying easily, feeling trapped or caught, blaming yourself for things, feeling lonely, feeling blue, worrying too much about things, feeling no interest in things, feeling hopeless about the future, feeling everything is an effort, and feeling worthless.

Both the unadjusted and adjusted analyses revealed a marginally significant difference in the prevalence of high SCL-90-R depression scores between Ranch Hands (13.3%) and Comparisons (16.1%) when examined across all occupations (Table 12-9(a,b): p=0.073, Est. RR=0.80; p=0.077, Adj. RR=0.79, respectively). In addition, a significant difference was found within the enlisted flyer stratum in both the unadjusted and adjusted analyses (Table 12-9(a,b): p=0.038, Est. RR=0.53; p=0.013, Adj. RR=0.45, respectively). The prevalence of high SCL-90-R depression scores was higher among Comparisons (21.4%) than Ranch Hands (12.7%) for this occupation. All remaining Model 1 contrasts, as well as the Model 2 analyses, were nonsignificant (Table 12-9(a–d): p>0.13).

Table 12-9. Analysis of SCL-90-R Depression

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***115 (13.3)***	***0.80 (0.62,1.02)***	***0.073***
	Comparison	***1,249***	***201 (16.1)***		
Officer	Ranch Hand	341	28 (8.2)	0.85 (0.52,1.39)	0.512
	Comparison	493	47 (9.5)		
Enlisted Flyer	Ranch Hand	150	19 (12.7)	0.53 (0.29,0.97)	0.038
	Comparison	187	40 (21.4)		
Enlisted Groundcrew	Ranch Hand	375	68 (18.1)	0.88 (0.63,1.23)	0.469
	Comparison	569	114 (20.0)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.79 (0.61,1.03)***	***0.077***
Officer	0.89 (0.54,1.46)	0.642
Enlisted Flyer	0.45 (0.24,0.84)	0.013
Enlisted Groundcrew	0.90 (0.64,1.28)	0.562

Table 12-9. Analysis of SCL-90-R Depression (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	22 (13.8)	1.10 (0.91,1.32)	0.345
Medium	161	23 (14.3)		
High	157	26 (16.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
471	0.84 (0.67,1.06)	0.138

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	194 (16.0)		
Background RH	381	43 (11.3)	0.70 (0.49,1.00)	0.052
Low RH	239	30 (12.6)	0.74 (0.49,1.12)	0.156
High RH	239	41 (17.2)	1.03 (0.71,1.50)	0.862
Low plus High RH	478	71 (14.9)	0.88 (0.65,1.18)	0.383

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 12-9. Analysis of SCL-90-R Depression (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,196		
Background RH	374	0.88 (0.60,1.27)	0.485
Low RH	236	0.78 (0.51,1.20)	0.256
High RH	235	0.74 (0.49,1.11)	0.142
Low plus High RH	471	0.76 (0.55,1.04)	0.087

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	29 (10.1)	1.15 (1.01,1.31)	0.040
Medium	287	38 (13.2)		
High	284	47 (16.6)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
845	0.97 (0.84,1.13)	0.712

[a] Relative risk for a twofold increase in 1987 dioxin.

The unadjusted Model 3 analysis revealed a marginally significant difference in the prevalence of high SCL-90-R depression scores among Ranch Hands in the background category (11.3%) and Comparisons (16.0%) (Table 12-9(e): p=0.052, Est. RR=0.70). All other unadjusted contrasts were nonsignificant (Table 12-9(e): p>0.15). The Model 3 adjusted analysis revealed a marginally significant difference among Ranch Hands in the combined low and high dioxin categories and Comparisons (Table 12-9(g): p=0.087, Adj. RR=0.76). The remaining adjusted contrasts were nonsignificant (Table 12-9(f): p>0.14).

A significant positive association between the 1987 dioxin levels and the prevalence of a high SCL-90-R depression score was found from the unadjusted analysis of Model 4 (Table 12-9(g): p=0.040, Est. RR=1.15). The association was nonsignificant after adjustments for covariates (Table 12-9(h): p=0.712).

12.2.2.2.3 SCL-90-R Hostility

The hostility dimension reflects thoughts, feelings, or actions that are characteristic of the negative affect state of anger. The selection of items includes all three modes of manifestation and reflects qualities such as aggression, irritability, rage, and resentment. The symptoms comprising the hostility dimension are feeling easily annoyed or irritated; having uncontrollable temper outbursts; having urges to beat, injure, or harm someone; having urges to break or smash things; getting into frequent arguments; and shouting or throwing things.

The analysis of SCL-90-R hostility showed no significant results for Models 1 and 2 (Table 12-10(a–d): p>0.12 for each analysis).

Table 12-10. Analysis of SCL-90-R Hostility

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***61 (7.0)***	***0.78 (0.56,1.08)***	***0.124***
	Comparison	***1,249***	***111 (8.9)***		
Officer	Ranch Hand	341	11 (3.2)	0.68 (0.33,1.42)	0.304
	Comparison	493	23 (4.7)		
Enlisted Flyer	Ranch Hand	150	11 (7.3)	0.63 (0.29,1.34)	0.228
	Comparison	187	21 (11.2)		
Enlisted Groundcrew	Ranch Hand	375	39 (10.4)	0.87 (0.57,1.32)	0.513
	Comparison	569	67 (11.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.81 (0.58,1.13)***	***0.217***
Officer	0.71 (0.34,1.49)	0.367
Enlisted Flyer	0.66 (0.30,1.45)	0.301
Enlisted Groundcrew	0.90 (0.59,1.39)	0.642

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	12 (7.5)	1.12 (0.88,1.42)	0.377
Medium	161	12 (7.5)		
High	157	15 (9.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 12-10. Analysis of SCL-90-R Hostility (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
471	0.94 (0.71,1.25)	0.692

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	107 (8.8)		
Background RH	381	22 (5.8)	0.66 (0.41,1.07)	0.090
Low RH	239	16 (6.7)	0.73 (0.42,1.26)	0.261
High RH	239	23 (9.6)	1.05 (0.65,1.70)	0.828
Low plus High RH	478	39 (8.2)	0.88 (0.60,1.30)	0.512

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,196		
Background RH	374	0.86 (0.52,1.40)	0.536
Low RH	236	0.80 (0.46,1.40)	0.440
High RH	235	0.84 (0.51,1.38)	0.488
Low plus High RH	471	0.82 (0.55,1.22)	0.333

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 12-10. Analysis of SCL-90-R Hostility (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	16 (5.6)	1.19 (1.01,1.41)	0.045
Medium	287	19 (6.6)		
High	284	26 (9.2)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
845	1.01 (0.84,1.23)	0.889

[a] Relative risk for a twofold increase in 1987 dioxin.

A marginally significant difference in the prevalence of high SCL-90-R hostility scores was found among Ranch Hands in the background dioxin category (5.8%) and Comparisons (8.8%) from the Model 3 unadjusted analysis (Table 12-10(e): p=0.090, Est. RR=0.66). After adjustment for covariates, the difference was nonsignificant (Table 12-10(f): p=0.536), as well as all other Model 3 contrasts (Table 12-10(e,f): p>0.26 for all remaining contrasts).

The Model 4 unadjusted analysis showed a significant positive association between the 1987 dioxin levels and the prevalence of high SCL-90-R hostility scores (Table 12-10(g): p=0.045, Est. RR=1.19). After covariates were included in the model, the association was nonsignificant (Table 12-10(h): p=0.889).

12.2.2.2.4 SCL-90-R Interpersonal Sensitivity

The interpersonal sensitivity dimension focuses on feelings of personal inadequacy and inferiority, particularly in comparison with others. Self-deprecation, feelings of uneasiness, and marked discomfort during interpersonal interactions are characteristic manifestations of this syndrome. In addition, individuals with high scores on interpersonal sensitivity report acute self-consciousness and negative expectations concerning the communications and interpersonal behaviors with others. The symptoms comprising the interpersonal sensitivity dimension are feeling critical of others, feeling shy or uneasy with the opposite sex, having feelings easily hurt, feeling others do not understand or are unsympathetic to, feeling that people are unfriendly or dislike you, feeling inferior to others, feeling uneasy when people are watching or talking about you, feeling very self-conscious with others, and feeling uncomfortable about eating or drinking in public.

The Model 1 unadjusted analysis of SCL-90-R interpersonal sensitivity revealed marginally significant differences between Ranch Hands and Comparisons examined across all occupational strata and within the enlisted flyer stratum (Table 12-11(a): p=0.066, Est. RR=0.80; p=0.072, Est. RR=0.59, respectively). The results remained marginally significant for the contrast of Ranch Hands and Comparisons across all occupations in the adjusted analysis and became significant for the enlisted flyer contrast (Table 12-11(b):

p=0.070, Adj. RR=0.79; p=0.029, Adj. RR=0.52, respectively). Both contrasts showed that Comparisons had an increased prevalence of high SCL-90-R interpersonal sensitivity scores over Ranch Hands (16.4% vs. 13.5% for all occupations combined and 22.5% vs. 14.7% for enlisted flyers). All other Model 1 contrasts were nonsignificant (Table 12-11(a,b): p>0.27 for all remaining contrasts).

Table 12-11. Analysis of SCL-90-R Interpersonal Sensitivity

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	**Group**	**n**	**Number (%) High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***866***	***117 (13.5)***	***0.80 (0.62,1.02)***	***0.066***
	Comparison	***1,249***	***205 (16.4)***		
Officer	Ranch Hand	341	25 (7.3)	0.90 (0.53,1.51)	0.679
	Comparison	493	40 (8.1)		
Enlisted Flyer	Ranch Hand	150	22 (14.7)	0.59 (0.34,1.05)	0.072
	Comparison	187	42 (22.5)		
Enlisted Groundcrew	Ranch Hand	375	70 (18.7)	0.83 (0.60,1.15)	0.272
	Comparison	569	123 (21.6)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	**Adjusted Relative Risk (95% C.I.)**	**p-Value**
All	***0.79 (0.61,1.02)***	***0.070***
Officer	0.93 (0.55,1.56)	0.772
Enlisted Flyer	0.52 (0.28,0.93)	0.029
Enlisted Groundcrew	0.86 (0.61,1.20)	0.366

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Number (%) High**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	160	27 (16.9)	0.98 (0.81,1.18)	0.798
Medium	161	26 (16.2)		
High	157	26 (16.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
471	0.78 (0.62,0.97)	0.026

[a] Relative risk for a twofold increase in initial dioxin.

Table 12-11. Analysis of SCL-90-R Interpersonal Sensitivity (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	198 (16.4)		
Background RH	381	37 (9.7)	0.57 (0.39,0.83)	0.003
Low RH	239	36 (15.1)	0.90 (0.61,1.32)	0.586
High RH	239	43 (18.0)	1.08 (0.75,1.56)	0.672
Low plus High RH	478	79 (16.5)	0.99 (0.74,1.31)	0.923

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,196		
Background RH	374	0.73 (0.49,1.07)	0.110
Low RH	236	0.92 (0.62,1.38)	0.698
High RH	235	0.77 (0.53,1.14)	0.190
Low plus High RH	471	0.84 (0.63,1.14)	0.270

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	28 (9.7)	1.12 (0.98,1.28)	0.090
Medium	287	39 (13.6)		
High	284	49 (17.3)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 12-11. Analysis of SCL-90-R Interpersonal Sensitivity (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
845	0.95 (0.82,1.10)	0.511

[a] Relative risk for a twofold increase in 1987 dioxin.

The Model 2 unadjusted analysis of the association between initial dioxin and SCL-90-R interpersonal sensitivity scores was nonsignificant (Table 12-11(c): p=0.798). After adjustment for covariates, the association became significant (Table 12-11(d): p=0.026, Adj. RR=0.78). The prevalence of high SCL-90-R interpersonal sensitivity scores decreased as initial dioxin increased.

A significant difference between Ranch Hands in the background dioxin category and Comparisons was found from the unadjusted Model 3 analysis of SCL-90-R interpersonal sensitivity (Table 12-11(e): p=0.003, Est. RR=0.57). The prevalence of high SCL-90-R scores was greater among Comparisons (16.4%) than among Ranch Hands in the background dioxin category (9.7%). All other Model 3 unadjusted contrasts, as well as all adjusted contrasts, were nonsignificant (Table 12-11(e,f): p≥0.11 for all remaining contrasts).

The result from the Model 4 unadjusted analysis of SCL-90-R interpersonal sensitivity was marginally significant, indicating a positive association with the 1987 dioxin levels (Table 12-11(g): p=0.090, Est. RR=1.12). After adjustment for covariates, the result became nonsignificant (Table 12-11(h): p=0.511).

12.2.2.2.5 SCL-90-R Obsessive-Compulsive Behavior

The obsessive-compulsive dimension reflects symptoms that are highly identified with the standard clinical syndrome of the same name. This measure focuses on thoughts, impulses, and actions that are experienced as unremitting and irresistible by the individual but are of an ego-alien or unwanted nature. Behaviors and experiences of a more general cognitive performance attenuation also are included in this measure. The symptoms comprising the obsessive-compulsive dimension are experiencing repeated unpleasant thoughts that won't leave the mind, having trouble remembering things, worrying about sloppiness or carelessness, feeling blocked in getting things done, having to do things very slowly to ensure correctness, having to check and double-check what is done, having difficulty making decisions, having mind go blank, having trouble concentrating, and having to repeat the same actions (e.g., touching, counting, washing).

All Model 1 and 2 analyses of SCL-90-R obsessive-compulsive behavior were nonsignificant, both unadjusted and adjusted for covariates (Table 12-12(a–d): p>0.12 for each analysis).

Table 12-12. Analysis of SCL-90-R Obsessive-Compulsive Behavior

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***121 (14.0)***	***0.83 (0.65,1.06)***	***0.125***
	Comparison	***1,249***	***205 (16.4)***		
Officer	Ranch Hand	341	30 (8.8)	0.92 (0.57,1.48)	0.718
	Comparison	493	47 (9.5)		
Enlisted Flyer	Ranch Hand	150	28 (18.7)	0.82 (0.48,1.40)	0.462
	Comparison	187	41 (21.9)		
Enlisted Groundcrew	Ranch Hand	375	63 (16.8)	0.78 (0.56,1.09)	0.150
	Comparison	569	117 (20.6)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.83 (0.65,1.07)***	***0.157***
Officer	0.95 (0.58,1.54)	0.824
Enlisted Flyer	0.77 (0.44,1.35)	0.365
Enlisted Groundcrew	0.81 (0.57,1.14)	0.225

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	26 (16.3)	1.02 (0.85,1.23)	0.854
Medium	161	27 (16.8)		
High	157	24 (15.3)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
471	0.89 (0.71,1.11)	0.286

[a] Relative risk for a twofold increase in initial dioxin.

Table 12-12. Analysis of SCL-90-R Obsessive-Compulsive Behavior (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	198 (16.4)		
Background RH	381	43 (11.3)	0.68 (0.48,0.97)	0.032
Low RH	239	38 (15.9)	0.96 (0.65,1.40)	0.821
High RH	239	39 (16.3)	0.96 (0.66,1.40)	0.831
Low plus High RH	478	77 (16.1)	0.96 (0.72,1.28)	0.773

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,196		
Background RH	374	0.84 (0.58,1.21)	0.340
Low RH	236	1.01 (0.68,1.50)	0.948
High RH	235	0.72 (0.48,1.07)	0.103
Low plus High RH	471	0.85 (0.63,1.15)	0.298

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	30 (10.4)	1.13 (1.00,1.29)	0.058
Medium	287	42 (14.6)		
High	284	48 (16.9)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 12-12. Analysis of SCL-90-R Obsessive-Compulsive Behavior (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
845	1.00 (0.87,1.16)	0.964

[a] Relative risk for a twofold increase in 1987 dioxin.

The Model 3 unadjusted analysis of SCL-90-R obsessive-compulsive behavior revealed a significant difference in the prevalence of high SCL-90-R scores between Ranch Hands in the background category (11.3%) and Comparisons (16.4%) (Table 12-12(e): p=0.032, Est. RR=0.68). The result was nonsignificant after adjustment for covariates (Table 12-12(f): p=0.340). All other Model 3 contrasts were also nonsignificant (Table 12-12(e,f): p>0.10 for all other contrasts).

A marginally significant positive association was found between the 1987 dioxin levels and the prevalence of high SCL-90-R obsessive-compulsive behavior scores from the unadjusted Model 4 analysis (Table 12-12(g): p=0.058, Est. RR=1.13). After adjustment for covariates, the association was nonsignificant (Table 12-12(h): p=0.964).

12.2.2.2.6 SCL-90-R Paranoid Ideation

The present dimension represents paranoid behavior fundamentally as a disordered mode of thinking. The cardinal characteristics of projective thought, hostility, suspiciousness, grandiosity, centrality, fear of loss of autonomy, and delusions are viewed as primary reflections of this disorder; item selection was oriented toward representing this conceptualization. The symptoms comprising the paranoid ideation dimension are feeling others are to blame for most of your troubles, feeling that most people cannot be trusted, feeling that you are watched or talked about by others, having ideas and beliefs that others do not share, not receiving proper credit from others for your achievements, and feeling that people will take advantage of you if you let them.

All results from the Model 1 and 2 analyses of SCL-90-R paranoid ideation were nonsignificant (Table 12-13(a–d): p>0.19 for each examination).

Table 12-13. Analysis of SCL-90-R Paranoid Ideation

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***57 (6.6)***	***0.92 (0.65,1.30)***	***0.627***
	Comparison	***1,249***	***89 (7.1)***		
Officer	Ranch Hand	341	8 (2.4)	0.77 (0.32,1.83)	0.547
	Comparison	493	15 (3.0)		
Enlisted Flyer	Ranch Hand	150	8 (5.3)	0.56 (0.24,1.34)	0.196
	Comparison	187	17 (9.1)		
Enlisted Groundcrew	Ranch Hand	375	41 (10.9)	1.10 (0.72,1.69)	0.652
	Comparison	569	57 (10.0)		

Table 12-13. Analysis of SCL-90-R Paranoid Ideation (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.98 (0.68,1.40)***	***0.898***
Officer	0.84 (0.35,2.03)	0.698
Enlisted Flyer	0.56 (0.23,1.37)	0.206
Enlisted Groundcrew	1.17 (0.76,1.81)	0.479

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	8 (5.0)	1.16 (0.91,1.47)	0.227
Medium	161	15 (9.3)		
High	157	16 (10.2)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
471	0.88 (0.66,1.17)	0.374

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	85 (7.0)		
Background RH	381	17 (4.5)	0.65 (0.38,1.10)	0.110
Low RH	239	13 (5.4)	0.75 (0.41,1.38)	0.357
High RH	239	26 (10.9)	1.56 (0.98,2.48)	0.062
Low plus High RH	478	39 (8.2)	1.08 (0.72,1.64)	0.703

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 12-13. Analysis of SCL-90-R Paranoid Ideation (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,196		
Background RH	374	0.90 (0.51,1.57)	0.702
Low RH	236	0.87 (0.47,1.61)	0.657
High RH	235	1.16 (0.71,1.89)	0.559
Low plus High RH	471	1.00 (0.65,1.54)	0.990

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	14 (4.9)	1.21 (1.02,1.45)	0.032
Medium	287	13 (4.5)		
High	284	29 (10.2)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
845	1.00 (0.82,1.20)	0.960

[a] Relative risk for a twofold increase in 1987 dioxin.

The Model 3 unadjusted analysis of SCL-90-R paranoid ideation revealed a marginally significant difference in the prevalence of high SCL-90-R scores among Ranch Hands in the high dioxin category (10.9%) and Comparisons (7.0%) (Table 12-13(e): p=0.062, Est. RR=1.56). All other unadjusted contrasts were nonsignificant (Table 12-13(e): p≥0.11). After covariate adjustment, all results were nonsignificant (Table 12-13(f): p>0.55 for each adjusted contrast).

A significant positive association between the prevalence of high SCL-90-R paranoid ideation scores and the 1987 dioxin levels was found in the Model 4 unadjusted analysis (Table 12-13(g): p=0.032, Est. RR=1.21). The result was nonsignificant after adjustment for covariates (Table 12-13(h): p=0.960).

12.2.2.2.7 SCL-90-R Phobic Anxiety

Phobic anxiety is defined as a persistent fear response to a specific person, place, object, or situation that is characterized as being irrational and disproportionate to the stimulus and which leads to avoidance or escape behavior. The items of the present dimension focus on the more pathognomonic and disruptive manifestations of phobic behavior. The symptoms comprising the phobic anxiety dimension are feeling afraid in open spaces or on the street; feeling afraid to go out of the house alone; feeling afraid to travel on buses, subways, or trains; having to avoid certain things, places, or activities because they are frightening; feeling uneasy in crowds, such as while shopping or at a movie; feeling nervous when left alone; and feeling afraid of fainting in public.

The Model 1 unadjusted and adjusted analyses of the officer stratum revealed that Comparisons had a marginally significant higher prevalence of high SCL-90-R phobic anxiety scores than Ranch Hands (5.7% vs. 2.9%) (Table 12-14(a,b): p=0.066, Est. RR=0.50; p=0.090, Adj. RR=0.53, respectively). All other Model 1 contrasts were nonsignificant (Table 12-14(a,b): p>0.13 for all remaining contrasts).

Table 12-14. Analysis of SCL-90-R Phobic Anxiety

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***85 (9.8)***	***0.93 (0.70,1.24)***	***0.615***
	Comparison	***1,249***	***131 (10.5)***		
Officer	Ranch Hand	341	10 (2.9)	0.50 (0.24,1.05)	0.066
	Comparison	493	28 (5.7)		
Enlisted Flyer	Ranch Hand	150	15 (10.0)	0.66 (0.34,1.29)	0.223
	Comparison	187	27 (14.4)		
Enlisted Groundcrew	Ranch Hand	375	60 (16.0)	1.24 (0.86,1.78)	0.258
	Comparison	569	76 (13.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.92 (0.68,1.24)***	***0.570***
Officer	0.53 (0.25,1.11)	0.090
Enlisted Flyer	0.59 (0.29,1.18)	0.136
Enlisted Groundcrew	1.24 (0.85,1.81)	0.270

Table 12-14. Analysis of SCL-90-R Phobic Anxiety (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	17 (10.6)	1.18 (0.97,1.44)	0.100
Medium	161	19 (11.8)		
High	157	26 (16.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
471	0.89 (0.70,1.12)	0.315

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	126 (10.4)		
Background RH	381	22 (5.8)	0.53 (0.33,0.85)	0.009
Low RH	239	25 (10.5)	1.00 (0.64,1.58)	0.986
High RH	239	37 (15.5)	1.57 (1.05,2.33)	0.027
Low plus High RH	478	62 (13.0)	1.25 (0.90,1.74)	0.177

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 12-14. Analysis of SCL-90-R Phobic Anxiety (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,196		
Background RH	374	0.65 (0.40,1.06)	0.086
Low RH	236	1.04 (0.65,1.67)	0.872
High RH	235	1.11 (0.72,1.70)	0.647
Low plus High RH	471	1.07 (0.76,1.52)	0.694

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	15 (5.2)	1.28 (1.11,1.48)	0.001
Medium	287	27 (9.4)		
High	284	42 (14.8)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
845	1.03 (0.88,1.21)	0.727

[a] Relative risk for a twofold increase in 1987 dioxin.

The unadjusted Model 2 analysis revealed a marginally significant positive association between initial dioxin and the prevalence of high SCL-90-R phobic anxiety scores (Table 12-14(c): p=0.100, Est. RR=1.18). After adjustment for covariates, the association was nonsignificant (Table 12-14(d): p=0.315, Adj. RR=0.89).

Significant differences among Comparisons and Ranch Hands in both the background and high dioxin categories were found from the unadjusted Model 3 analysis of SCL-90-R phobic anxiety (Table 12-14(e): p=0.009, Est. RR=0.53; p=0.027, Est. RR=1.57, respectively). Higher SCL-90-R phobic anxiety scores were more prevalent among Comparisons than Ranch Hands in the background dioxin category (10.4% vs. 5.8%). Higher phobic anxiety scores were more prevalent among Ranch Hands in the high dioxin category than Comparisons (15.5% vs. 10.4%). Results were marginally significant for

the adjusted Ranch Hand background dioxin category contrast with Comparisons and nonsignificant for the adjusted contrast of Ranch Hands in the high dioxin category with Comparisons (Table 12-14(f): p=0.086, Adj. RR=0.65; p=0.647, respectively). All other Model 3 contrasts were nonsignificant (Table 12-14(e,f): p>0.17 for all remaining contrasts).

The results from the Model 4 unadjusted analysis revealed a significant positive association between the 1987 dioxin levels and the SCL-90-R phobic anxiety scores (Table 12-14(g): p=0.001, Est. RR=1.28). The association was nonsignificant after adjustment for covariates (Table 12-14(h): p=0.727).

12.2.2.2.8 SCL-90-R Psychoticism

The psychoticism scale was developed in a fashion to represent the construct as a continuous dimension of human experience. Items indicative of a withdrawn, isolated, schizoid lifestyle were included, as were first-rank symptoms of schizophrenia, such as hallucinations and thought-broadcasting. The symptoms comprising the psychoticism dimension are having the idea that someone else can control your thoughts, hearing voices that other people do not hear, believing that other people are aware of your private thoughts, having thoughts that are not your own, feeling lonely even when you are with people, having thoughts about sex that bother you a lot, believing that you should be punished for your sins, thinking that something serious is wrong with your body, never feeling close to another person, and thinking that something is wrong with your mind.

The contrast combining all occupations from the Model 1 unadjusted analysis of SCL-90-R psychoticism revealed a marginally significant difference in the prevalence of higher scores (Table 12-15(a): p=0.084, Est. RR=0.80). The prevalence of high psychoticism scores was greater for Comparisons than for Ranch Hands (14.7% vs. 12.1%). The results were nonsignificant in the adjusted analysis, as well as for all other Model 1 contrasts (Table 12-15(a,b): p>0.11 for all remaining contrasts).

Table 12-15. Analysis of SCL-90-R Psychoticism

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***105 (12.1)***	***0.80 (0.62,1.03)***	***0.084***
	Comparison	***1,249***	***184 (14.7)***		
Officer	Ranch Hand	341	21 (6.2)	0.65 (0.38,1.12)	0.121
	Comparison	493	45 (9.1)		
Enlisted Flyer	Ranch Hand	150	19 (12.7)	0.73 (0.39,1.35)	0.317
	Comparison	187	31 (16.6)		
Enlisted Groundcrew	Ranch Hand	375	65 (17.3)	0.90 (0.64,1.26)	0.522
	Comparison	569	108 (19.0)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.81 (0.62,1.06)***	***0.116***
Officer	0.68 (0.39,1.17)	0.162
Enlisted Flyer	0.67 (0.36,1.27)	0.223
Enlisted Groundcrew	0.92 (0.65,1.31)	0.651

Table 12-15. Analysis of SCL-90-R Psychoticism (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	20 (12.5)	1.19 (0.99,1.44)	0.065
Medium	161	26 (16.2)		
High	157	25 (15.9)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
471	0.98 (0.78,1.22)	0.838

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	176 (14.5)		
Background RH	381	33 (8.7)	0.58 (0.39,0.86)	0.006
Low RH	239	28 (11.7)	0.77 (0.51,1.18)	0.237
High RH	239	43 (18.0)	1.25 (0.86,1.81)	0.235
Low plus High RH	478	71 (14.9)	0.98 (0.73,1.33)	0.914

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 12-15. Analysis of SCL-90-R Psychoticism (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,196		
Background RH	374	0.71 (0.47,1.07)	0.104
Low RH	236	0.83 (0.53,1.28)	0.394
High RH	235	0.95 (0.64,1.40)	0.786
Low plus High RH	471	0.88 (0.65,1.21)	0.447

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	24 (8.3)	1.24 (1.08,1.42)	0.002
Medium	287	30 (10.5)		
High	284	50 (17.6)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
845	1.06 (0.91,1.23)	0.484

[a] Relative risk for a twofold increase in 1987 dioxin.

The Model 2 unadjusted analysis revealed a marginally significant positive association between initial dioxin and SCL-90-R psychoticism scores (Table 12-15(c): p=0.065, Est. RR=1.19). After adjustment for covariates, the association was nonsignificant (Table 12-15(d): p=0.838).

A significant difference in the prevalence of high SCL-90-R psychoticism scores was found in the unadjusted Model 3 analysis between Ranch Hands in the background category (8.7%) and Comparisons (14.5%) (Table 12-15(e): p=0.006, Est. RR=0.58). Results became nonsignificant after covariate adjustment (Table 12-15(f): p=0.104). All other Model 3 contrasts were nonsignificant (Table 12-15(e,f): p>0.23 for all remaining contrasts).

The positive association between the 1987 dioxin levels and the SCL-90-R psychoticism scores was significant in the Model 4 unadjusted analysis (Table 12-15(g): p=0.002, Est. RR=1.24). The result became nonsignificant after covariate adjustment (Table 12-15(h): p=0.484).

12.2.2.2.9 SCL-90-R Somatization

The somatization dimension reflects distress arising from perceptions of bodily dysfunction. Complaints focusing on cardiovascular, gastrointestinal, respiratory, and other systems with strong autonomic mediation are included. Headaches, pain, and discomfort of the gross musculature and additional somatic equivalents of anxiety are components of the definition. These symptoms and signs have all been demonstrated to have high prevalence in disorders demonstrated to have a functional etiology, although all may be reflections of true physical disease. The symptoms comprising the somatization dimension are headaches, faintness or dizziness, pains in heart or chest, pains in lower back, nausea or upset stomach, soreness of muscles, trouble getting breath, hot or cold spells, numbness or tingling in parts of body, lump in throat, weakness in parts of body, and heavy feelings in arms or legs.

All Model 1 unadjusted and adjusted results from the analysis of SCL-90-R somatization were nonsignificant (Table 12-16(a,b): p>0.13 for each contrast).

Table 12-16. Analysis of SCL-90-R Somatization

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***143 (16.5)***	***1.03 (0.82,1.30)***	***0.797***
	Comparison	***1,249***	***201 (16.1)***		
Officer	Ranch Hand	341	25 (7.3)	1.00 (0.59,1.71)	0.987
	Comparison	493	36 (7.3)		
Enlisted Flyer	Ranch Hand	150	33 (22.0)	0.73 (0.44,1.21)	0.223
	Comparison	187	52 (27.8)		
Enlisted Groundcrew	Ranch Hand	375	85 (22.7)	1.18 (0.86,1.62)	0.300
	Comparison	569	113 (19.9)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.02 (0.80,1.31)***	***0.847***
Officer	1.02 (0.60,1.74)	0.948
Enlisted Flyer	0.67 (0.40,1.13)	0.133
Enlisted Groundcrew	1.22 (0.88,1.70)	0.232

Table 12-16. Analysis of SCL-90-R Somatization (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	34 (21.3)	0.98 (0.83,1.17)	0.840
Medium	161	33 (20.5)		
High	157	31 (19.8)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
471	0.76 (0.62,0.94)	0.010

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	194 (16.0)		
Background RH	381	44 (11.6)	0.71 (0.50,1.01)	0.056
Low RH	239	48 (20.1)	1.31 (0.92,1.86)	0.136
High RH	239	50 (20.9)	1.34 (0.95,1.91)	0.098
Low plus High RH	478	98 (20.5)	1.33 (1.01,1.74)	0.042

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 12-16. Analysis of SCL-90-R Somatization (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Comparison	1,196		
Background RH	374	0.92 (0.63,1.34)	0.669
Low RH	236	1.36 (0.93,1.97)	0.108
High RH	235	0.92 (0.63,1.33)	0.643
Low plus High RH	471	1.11 (0.84,1.48)	0.457

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**	
1987 Dioxin	**n**	**Number (%) High**	**Estimated Relative Risk (95% C.I.)[a]**	**p-Value**
Low	288	30 (10.4)	1.16 (1.03,1.31)	0.013
Medium	287	51 (17.8)		
High	284	61 (21.5)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
845	0.95 (0.83,1.09)	0.458

[a] Relative risk for a twofold increase in 1987 dioxin.

The unadjusted analysis of the association between initial dioxin (Model 2) and the prevalence of SCL-90-R somatization showed no significant results (Table 12-16(c): p=0.840). After adjustment for covariates, the association became significant and negative (Table 12-16(d): p=0.010, Adj. RR=0.76). As initial dioxin increased, the prevalence of high somatization scores decreased.

The unadjusted Model 3 analysis revealed a marginally significant difference in the prevalence of high SCL-90-R somatization scores between Ranch Hands in the background dioxin category (11.6%) and Comparisons (16.0%) (Table 12-16(e): p=0.056, Est. RR=0.71). Results were also marginally significant for the Ranch Hands in the high dioxin category contrast, where more Ranch Hands (20.9%) than Comparisons (16.0%) had a high somatization score (Table 12-16(e): p=0.098, Est. RR=1.34). Similarly, results were significant for the low and high dioxin categories combined, where more Ranch Hands

(20.5%) had a high somatization score than did Comparisons (16.0%) (Table 12-16(e): p=0.042, Est. RR=1.33). All contrasts were nonsignificant when adjusted for covariates (Table 12-16(f): p>0.10).

The Model 4 unadjusted analysis revealed a significant positive association between the 1987 dioxin levels and the prevalence of SCL-90-R somatization scores (Table 12-16(g): p=0.013, Est. RR=1.16). The result was nonsignificant after covariate adjustment (Table 12-16(h): p=0.458).

12.2.2.2.10 SCL-90-R Global Severity Index (GSI)

The GSI represents the best single indicator of the current level or depth of the disorder and should be used in most instances where a single summary measure is required. The GSI combines information on numbers of symptoms and intensity of perceived distress.

A marginally significant difference between Ranch Hand and Comparison enlisted flyers was found from the Model 1 unadjusted and adjusted analyses of SCL-90-R GSI (Table 12-17(a,b): p=0.091, Est. RR=0.61; p=0.066, Adj. RR=0.57, respectively). More Comparison enlisted flyers (21.9%) than Ranch Hand enlisted flyers (14.7%) displayed high GSI scores. All other Model 1 contrasts and each Model 2 analysis were nonsignificant (Table 12-17(a–d): p>0.15 for each analysis).

Table 12-17. Analysis of SCL-90-R Global Severity Index (GSI)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***118 (13.6)***	***0.85 (0.67,1.09)***	***0.204***
	Comparison	***1,249***	***195 (15.6)***		
Officer	Ranch Hand	341	23 (6.7)	0.89 (0.52,1.53)	0.676
	Comparison	493	37 (7.5)		
Enlisted Flyer	Ranch Hand	150	22 (14.7)	0.61 (0.35,1.08)	0.091
	Comparison	187	41 (21.9)		
Enlisted Groundcrew	Ranch Hand	375	73 (19.5)	0.93 (0.67,1.29)	0.681
	Comparison	569	117 (20.6)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.87 (0.67,1.13)***	***0.285***
Officer	0.93 (0.54,1.61)	0.805
Enlisted Flyer	0.57 (0.32,1.04)	0.066
Enlisted Groundcrew	0.97 (0.70,1.36)	0.876

Table 12-17. Analysis of SCL-90-R Global Severity Index (GSI) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	23 (14.4)	1.08 (0.90,1.29)	0.415
Medium	161	30 (18.6)		
High	157	29 (18.5)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
471	0.86 (0.69,1.06)	0.157

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	185 (15.3)		
Background RH	381	35 (9.2)	0.59 (0.40,0.87)	0.007
Low RH	239	35 (14.6)	0.94 (0.63,1.39)	0.754
High RH	239	47 (19.7)	1.30 (0.91,1.86)	0.153
Low plus High RH	478	82 (17.2)	1.10 (0.83,1.47)	0.500

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 12-17. Analysis of SCL-90-R Global Severity Index (GSI) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,196		
Background RH	374	0.77 (0.51,1.15)	0.200
Low RH	236	1.03 (0.69,1.55)	0.877
High RH	235	0.93 (0.64,1.36)	0.711
Low plus High RH	471	0.98 (0.73,1.32)	0.897

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	23 (8.0)	1.24 (1.09,1.41)	0.001
Medium	287	38 (13.2)		
High	284	56 (19.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
845	1.04 (0.90,1.21)	0.555

[a] Relative risk for a twofold increase in 1987 dioxin.

The unadjusted analysis of Model 3 revealed an increased prevalence of high SCL-90-R GSI scores among Comparisons (15.3%) than among Ranch Hands in the background category (9.2%) (Table 12-17(e): p=0.007, Est. RR=0.59). Analysis of this contrast when adjusted for covariates was nonsignificant (p=0.200), as were all other Model 3 contrasts (Table 12-17(f): p>0.15 for all other contrasts).

Examination of the association between 1987 dioxin levels and the prevalence of high SCL-90-R GSI scores revealed a significant positive result (Table 12-17(g): p=0.001, Est. RR=1.24). The prevalence of high GSI scores increased as 1987 dioxin levels increased. The adjusted analysis was nonsignificant (Table 12-17(h): p=0.555).

12.2.2.2.11 SCL-90-R Positive Symptom Total (PST)

The PST is simply a count of the number of symptoms the participant reports as experiencing to any degree. When used configurally in conjunction with the GSI, information on style of response and numbers of symptoms endorsed can be helpful in appreciating the clinical picture.

The results from both the unadjusted and adjusted Model 1 analyses of SCL-90-R PST across all occupations showed a marginally significant difference between Ranch Hands and Comparisons (Table 12-18(a,b): p=0.076, Est. RR=0.81; p=0.083, Adj. RR=0.80, respectively). The prevalence of high SCL-90-R PST scores was greater among Comparisons (17.1%) than among Ranch Hands (14.2%). All other Model 1 contrasts were nonsignificant (Table 12-18(a,b): p>0.16 for all remaining contrasts).

Table 12-18. Analysis of SCL-90-R Positive Symptom Total (PST)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***123 (14.2)***	***0.81 (0.63,1.02)***	***0.076***
	Comparison	***1,249***	***213 (17.1)***		
Officer	Ranch Hand	341	25 (7.3)	0.77 (0.46,1.28)	0.310
	Comparison	493	46 (9.3)		
Enlisted Flyer	Ranch Hand	150	26 (17.3)	0.72 (0.42,1.25)	0.245
	Comparison	187	42 (22.5)		
Enlisted Groundcrew	Ranch Hand	375	72 (19.2)	0.84 (0.61,1.17)	0.306
	Comparison	569	125 (22.0)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.80 (0.62,1.03)***	***0.083***
Officer	0.80 (0.48,1.33)	0.382
Enlisted Flyer	0.67 (0.38,1.18)	0.168
Enlisted Groundcrew	0.86 (0.61,1.20)	0.365

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	23 (14.4)	1.04 (0.87,1.25)	0.647
Medium	161	34 (21.1)		
High	157	28 (17.8)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 12-18. Analysis of SCL-90-R Positive Symptom Total (PST) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
471	0.82 (0.66,1.02)	0.067

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	204 (16.9)		
Background RH	381	36 (9.5)	0.54 (0.37,0.78)	0.001
Low RH	239	40 (16.7)	0.98 (0.68,1.42)	0.921
High RH	239	45 (18.8)	1.10 (0.77,1.58)	0.604
Low plus High RH	478	85 (17.8)	1.04 (0.79,1.37)	0.790

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,196		
Background RH	374	0.67 (0.45,0.99)	0.045
Low RH	236	1.04 (0.71,1.54)	0.830
High RH	235	0.78 (0.53,1.15)	0.209
Low plus High RH	471	0.90 (0.67,1.21)	0.496

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 12-18. Analysis of SCL-90-R Positive Symptom Total (PST) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	26 (9.0)	1.22 (1.07,1.38)	0.003
Medium	287	37 (12.9)		
High	284	58 (20.4)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
Analysis Results for Log_2 (1987 Dioxin + 1)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
845	1.02 (0.89,1.18)	0.764

[a] Relative risk for a twofold increase in 1987 dioxin.

The association between initial dioxin and SCL-90-R PST was nonsignificant in the Model 2 unadjusted analysis but marginally significant in the adjusted analysis (Table 12-18(c,d): p=0.647, Est. RR=1.04; p=0.067, Adj. RR=0.82, for the unadjusted and adjusted analyses, respectively). After adjustment, PST scores decreased with initial dioxin.

The unadjusted and adjusted results from the Model 3 analysis of SCL-90-R PST displayed a significant difference in the prevalence of high SCL-90-R PST scores between Ranch Hands in the background category (9.5%) and Comparisons (16.9%) (Table 12-18(e,f): p=0.001, Est. RR=0.54; p=0.045, Adj. RR=0.67, respectively). All other Model 3 contrasts were nonsignificant (Table 12-18(e,f): p>0.20 for all remaining contrasts).

The Model 4 unadjusted analysis showed a significant positive association between 1987 dioxin levels and the prevalence of high SCL-90-R PST scores (Table 12-18(g): p=0.003, Est. RR=1.22). After adjustment for covariates, the association was nonsignificant (Table 12-18(h): p=0.764).

12.2.2.2.12 SCL-90-R Positive Symptom Distress Index (PSDI)

The PSDI is a pure intensity measure, in a sense, "corrected" for numbers of symptoms. It functions primarily as a measure of response style in the sense of communicating whether the patient is "augmenting" or "attenuating" symptomatic distress in his style of reporting his disorder.

All results from the analysis of SCL-90-R PSDI were nonsignificant for Models 1, 2, and 4 (Table 12-19(a–d,g–h): p>0.10 for each Model 1, 2, and 4 analysis).

Table 12-19. Analysis of SCL-90-R Positive Symptom Distress Index (PSDI)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***69 (8.0)***	***1.20 (0.86,1.67)***	***0.280***
	Comparison	***1,249***	***84 (6.7)***		
Officer	Ranch Hand	341	14 (4.1)	1.20 (0.58,2.47)	0.622
	Comparison	493	17 (3.5)		
Enlisted Flyer	Ranch Hand	150	13 (8.7)	0.84 (0.40,1.76)	0.642
	Comparison	187	19 (10.2)		
Enlisted Groundcrew	Ranch Hand	375	42 (11.2)	1.37 (0.88,2.12)	0.158
	Comparison	569	48 (8.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.20 (0.86,1.69)***	***0.283***
Officer	1.29 (0.62,2.68)	0.495
Enlisted Flyer	0.78 (0.36,1.66)	0.513
Enlisted Groundcrew	1.37 (0.88,2.12)	0.165

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	14 (8.8)	1.00 (0.79,1.26)	0.992
Medium	161	20 (12.4)		
High	157	13 (8.3)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.
Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
471	0.80 (0.61,1.05)	0.107

[a] Relative risk for a twofold increase in initial dioxin.

Table 12-19. Analysis of SCL-90-R Positive Symptom Distress Index (PSDI) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	78 (6.4)		
Background RH	381	22 (5.8)	0.90 (0.55,1.47)	0.671
Low RH	239	19 (8.0)	1.25 (0.74,2.11)	0.399
High RH	239	28 (11.7)	1.91 (1.21,3.02)	0.006
Low plus High RH	478	47 (9.8)	1.55 (1.05,2.27)	0.026

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,196		
Background RH	374	1.16 (0.70,1.92)	0.572
Low RH	236	1.31 (0.77,2.23)	0.325
High RH	235	1.38 (0.85,2.23)	0.191
Low plus High RH	471	1.34 (0.91,1.99)	0.143

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	16 (5.6)	1.13 (0.97,1.33)	0.130
Medium	287	21 (7.3)		
High	284	32 (11.3)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 12-19. Analysis of SCL-90-R Positive Symptom Distress Index (PSDI) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
845	0.96 (0.81,1.15)	0.675

[a] Relative risk for a twofold increase in 1987 dioxin.

The unadjusted Model 3 analysis revealed significant differences between Comparisons and Ranch Hands in both the high dioxin category and the low and high dioxin categories combined (Table 12-19(e): p=0.006, Est. RR=1.91; p=0.026, Est. RR=1.55, respectively). Both contrasts found more Ranch Hands (11.7% and 9.8%, respectively) than Comparisons (6.4%) with a high SCL-90-R PSDI score. Each contrast was nonsignificant in the adjusted analysis, as were all other Model 3 contrasts (Table 12-19(f): p>0.14 for all other contrasts).

12.3 DISCUSSION

Neuropsychiatric symptoms are encountered commonly in clinical practice and challenge the primary care physician to distinguish those that reflect primary psychological disorders from those secondary to an underlying medical condition. Anxiety and depression, for example, are frequently associated with organic illness, whether established or perceived, and often complicate both accurate diagnosis and response to therapy.

In behavioral medical practice, standardized interview protocols and testing instruments are well established in the assessment of emotional status and cognitive function. The psychological assessment protocols used in the baseline and 1985 follow-up examinations included the WAIS, the MMPI, the CI, and the CMI. The negative reaction of participants to the burdensome length and repetition of these instruments led to the introduction at the 1987 examinations of the more economical SCL-90-R and the MCMI.

In their published reviews of the world's literature, *Veterans and Agent Orange* (33, 34), The Institute of Medicine concluded that there was insufficient evidence to link herbicide exposure with neuropsychiatric and cognitive disorders. Among the most important methodological limitations cited was the possibility that a true psychological effect may be below the power of epidemiological studies to detect, particularly given the time lapse between exposure and testing. Other limitations include the confounding by the effects of combat stress and, as noted above in the introduction to the psychological assessment, the significant association of psychological symptoms with the self-perception of exposure.

Analyses of the 1997 psychometric data yielded few significant results, most of which were limited to diagnoses established by a medical records review. Although the overall prevalence of the five diagnoses was similar in each cohort, "other neuroses" occurred significantly more often in Ranch Hand enlisted groundcrew than in Comparisons (64.7% vs. 57.1%), becoming even more significant after adjustment for covariates. Evidence for a dioxin effect was noted in Model 3 as "other neuroses" occurred significantly more often in Ranch Hands in the high and low initial serum dioxin categories relative to Comparisons in both the unadjusted and adjusted analyses. Further, with respect to 1987 serum dioxin levels, a dose-response pattern was noted with a prevalence of 45.0 percent, 53.5 percent, and 64.9 percent, respectively, in the low, medium, and high dioxin categories. After adjustment for covariates, the effect was no longer significant.

In contrast to the 1992 examination results noted above, analyses of the SCL-90-R indices yielded no significant group or occupational differences between the Ranch Hand and Comparison cohorts, nor were there any significant associations with either the extrapolated initial or 1987 serum dioxin levels.

12.4 SUMMARY

Five psychological disorders verified by a medical records review and 12 measures from the SCL-90-R inventory were examined in the psychology assessment. The SCL-90-R consisted of nine primary symptom dimensions and three broad indices of psychological distress. Each endpoint was examined for a significant association, both unadjusted and adjusted for covariates, with group (Model 1), initial dioxin (Model 2), categorized dioxin (Model 3), and the 1987 dioxin levels (Model 4).

12.4.1 Model 1: Group Analysis

Differences between Ranch Hands and Comparisons were examined, both across all occupations and within each occupational stratum, for the psychology endpoints described above. The results are summarized and presented in Table 12-20. In enlisted groundcrew, a significantly greater percentage of Ranch Hands than Comparisons had a history of other neuroses for both the unadjusted and adjusted analyses. Other variables displaying either significant or marginally significant results from the SCL-90-R were anxiety, depression, interpersonal sensitivity, phobic anxiety, global severity index, and positive symptom total. These results were found from the analysis combining all occupations or from the officer or enlisted flyer strata. The analyses showed a greater percentage of Comparisons than Ranch Hands with high SCL-90-R scores.

Table 12-20. Summary of Group Analysis (Model 1) for Psychological Variables (Ranch Hands vs. Comparisons)

	UNADJUSTED			
Variable	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Medical Records				
Psychoses	NS	NS	NS	ns
Alcohol Dependence	NS	ns	NS	NS
Drug Dependence	ns	ns	--	NS
Anxiety	NS	ns	NS	NS
Other Neuroses	NS	ns*	NS	+0.021
Psychological Examination (SCL-90-R)				
Anxiety	ns	ns	ns	ns
Depression	ns*	ns	−0.038	ns
Hostility	ns	ns	ns	ns
Interpersonal Sensitivity	ns*	ns	ns*	ns
Obsessive-Compulsive Behavior	ns	ns	ns	ns
Paranoid Ideation	ns	ns	ns	NS
Phobic Anxiety	ns	ns*	ns	NS
Psychoticism	ns*	ns	ns	ns
Somatization	NS	NS	ns	NS
Global Severity Index (GSI)	ns	ns	ns*	ns
Positive Symptom Total (PST)	ns*	ns	ns	ns
Positive Symptom Distress Index (PSDI)	NS	NS	ns	NS

Table 12-20. Summary of Group Analysis (Model 1) for Psychological Variables (Ranch Hands vs. Comparisons) (Continued)

Note: NS or ns: Not significant (p>0.10).
ns*: Marginally significant (0.05<p≤0.10).
+: Relative risk ≥1.00.
–: Relative risk <1.00.
--: Analysis not performed because of the sparse number of participants with a drug dependence.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00. A lowercase "ns" denotes relative risk less than 1.00.

	ADJUSTED			
Variable	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Medical Records				
Psychoses	NS	NS	NS	ns
Alcohol Dependence	NS	ns	ns	NS
Drug Dependence	ns	--	--	ns
Anxiety	NS	ns	NS	NS
Other Neuroses	NS	ns	NS	+0.011
Psychological Examination (SCL-90-R)				
Anxiety	ns	ns	ns*	NS
Depression	ns*	ns	–0.013	ns
Hostility	ns	ns	ns	ns
Interpersonal Sensitivity	ns*	ns	–0.029	ns
Obsessive-Compulsive Behavior	ns	ns	ns	ns
Paranoid Ideation	ns	ns	ns	NS
Phobic Anxiety	ns	ns*	ns	NS
Psychoticism	ns	ns	ns	ns
Somatization	NS	NS	ns	NS
Global Severity Index (GSI)	ns	ns	ns*	ns
Positive Symptom Total (PST)	ns*	ns	ns	ns
Positive Symptom Distress Index (PSDI)	NS	NS	ns	NS

Note: NS or ns: Not significant (p>0.10).
ns*: Marginally significant (0.05<p≤0.10).
+: Relative risk ≥1.00.
–: Relative risk <1.00.
--: Analysis not performed because of the sparse number of participants with a drug dependence.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00. A lowercase "ns" denotes relative risk less than 1.00.

12.4.2 Model 2: Initial Dioxin Analysis

Associations between initial dioxin and each psychological endpoint were examined. The unadjusted analyses displayed only two marginally significant associations, both of which indicated more high SCL-90-R scores as initial dioxin increased. The association became nonsignificant in the adjusted analysis. Adjusted analyses of SCL-90-R anxiety, interpersonal sensitivity, and somatization revealed significant associations with initial dioxin, but high SCL-90-R scores decreased as initial dioxin increased. A marginally significant association was found between initial dioxin and the SCL-90-R positive symptom total, but high positive symptom total scores decreased as initial dioxin increased. The results of the initial dioxin analyses are shown in Table 12-21.

Table 12-21. Summary of Initial Dioxin Analysis (Model 2) for Psychological Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Psychoses	ns	ns
Alcohol Dependence	NS	NS
Drug Dependence	--	--
Anxiety	NS	ns
Other Neuroses	NS	ns
Psychological Examination (SCL-90-R)		
Anxiety	ns	–0.016
Depression	NS	ns
Hostility	NS	ns
Interpersonal Sensitivity	ns	–0.026
Obsessive-Compulsive Behavior	NS	ns
Paranoid Ideation	NS	ns
Phobic Anxiety	NS*	ns
Psychoticism	NS*	ns
Somatization	ns	–0.010
Global Severity Index (GSI)	NS	ns
Positive Symptom Total (PST)	NS	ns*
Positive Symptom Distress Index (PSDI)	NS	ns

Note: NS or ns: Not significant (p>0.10).
NS* or ns*: Marginally significant (0.05<p≤0.10).
–: Relative risk <1.00.
--: Analysis not performed because of the sparse number of participants with a drug dependence.
P-value given if p≤0.05.
A capital "NS" denotes a relative risk of 1.00. A lowercase "ns" denotes relative risk less than 1.00.

12.4.3 Model 3: Categorized Dioxin Analysis

Differences between Ranch Hands, categorized by dioxin levels, and Comparisons in the history of psychological disorders and the prevalence of high SCL-90-R scores were examined. A summary of the analyses is given in Table 12-22. Several significant and marginally significant results were found from the unadjusted analysis within each categorization of dioxin. Each result became nonsignificant after covariate adjustment, except for the analyses of other neuroses and SCL-90-R positive symptom total. In addition, the significant result from the unadjusted analysis of SCL-90-R phobic anxiety, which found a larger percentage of Comparisons than background Ranch Hands with high scores, became marginally

significant in the adjusted analysis. Ranch Hands in the low dioxin category and the low and high dioxin categories combined displayed a significantly higher prevalence of other neuroses than Comparisons in both the unadjusted and adjusted analyses. For the adjusted analysis of the SCL-90-R positive symptom total, a significant difference between Ranch Hands in the background category and Comparisons was found where Comparisons had the greater percentage of high SCL-90-R T-scores.

Table 12-22. Summary of Categorized Dioxin Analysis (Model 3) for Psychological Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Medical Records				
Psychoses	ns	NS	NS	NS
Alcohol Dependence	ns	NS	NS	NS
Drug Dependence	NS	ns	ns	ns
Anxiety	ns*	NS	NS	NS
Other Neuroses	–0.018	+0.041	+0.008	+0.002
Psychological Examination (SCL-90-R)				
Anxiety	ns*	ns	NS	NS
Depression	ns*	ns	NS	ns
Hostility	ns*	ns	NS	ns
Interpersonal Sensitivity	–0.003	ns	NS	ns
Obsessive-Compulsive Behavior	–0.032	ns	ns	ns
Paranoid Ideation	ns	ns	NS*	NS
Phobic Anxiety	–0.009	NS	+0.027	NS
Psychoticism	–0.006	ns	NS	ns
Somatization	ns*	NS	NS*	+0.042
Global Severity Index (GSI)	–0.007	ns	NS	NS
Positive Symptom Total (PST)	–0.001	ns	NS	NS
Positive Symptom Distress Index (PSDI)	ns	NS	+0.006	+0.026

Note: NS or ns: Not significant (p>0.10).
NS* or ns*: Marginally significant (0.05<p≤0.10).
+: Relative risk ≥1.00.
–: Relative risk <1.00.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater. A lowercase "ns" denotes relative risk less than 1.00.

Variable	ADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Medical Records				
Psychoses	ns	NS	ns	NS
Alcohol Dependence	NS	NS	NS	NS
Drug Dependence	NS	--	--	--
Anxiety	ns	NS	ns	ns

Table 12-22. Summary of Categorized Dioxin Analysis (Model 3) for Psychological Variables (Ranch Hands vs. Comparisons) (Continued)

Variable	ADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Other Neuroses	ns	+0.036	NS	+0.038
Psychological Examination (SCL-90-R)				
Anxiety	ns	NS	ns	ns
Interpersonal Sensitivity	ns	ns	ns	ns
Obsessive-Compulsive Behavior	ns	NS	ns	ns
Paranoid Ideation	ns	ns	NS	NS
Phobic Anxiety	ns*	NS	NS	NS
Psychoticism	ns	ns	ns	ns
Somatization	ns	NS	ns	NS
Global Severity Index (GSI)	ns	NS	ns	ns
Positive Symptom Total (PST)	–0.045	NS	ns	ns
Positive Symptom Distress Index (PSDI)	NS	NS	NS	NS

Note: NS or ns: Not significant (p>0.10).
ns*: Marginally significant (0.05<p≤0.10).
+: Relative risk ≥1.00.
–: Relative risk <1.00.
--: Analysis not performed because of the sparse number of participants with a drug dependence.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00. A lowercase "ns" denotes relative risk less than 1.00.

12.4.4 Model 4: 1987 Dioxin Level Analysis

The relation between the 1987 dioxin levels and the psychological endpoints was examined. Unadjusted analyses revealed significant or marginally significant associations for a history of anxiety and other neuroses and for most of the SCL-90-R measures. These associations indicated that disorders or high SCL-90-R scores increased as 1987 dioxin increased. After adjustment for covariates, all results became nonsignificant. A summary of the analyses is given in Table 12-23.

Table 12-23. Summary of 1987 Dioxin Analysis (Model 4) for Psychological Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Psychoses	NS	NS
Alcohol Dependence	NS	ns
Drug Dependence	ns	ns
Anxiety	+0.011	ns
Other Neuroses	+<0.001	NS
Psychological Examination (SCL-90-R)		
Anxiety	NS*	ns
Interpersonal Sensitivity	NS*	ns
Obsessive-Compulsive Behavior	NS*	NS

Table 12-23. Summary of 1987 Dioxin Analyses (Model 4) for Psychological Variables (Ranch Hands Only) (Continued)

Variable	Unadjusted	Adjusted
Paranoid Ideation	+0.032	NS
Phobic Anxiety	+0.001	NS
Psychoticism	+0.002	NS
Somatization	+0.013	ns
Global Severity Index (GSI)	+0.001	NS
Positive Symptom Total (PST)	+0.003	NS
Positive Symptom Distress Index (PSDI)	NS	ns

Note: NS or ns: Not significant (p>0.10).
NS*: Marginally significant (0.05<p≤0.10).
+: Relative risk ≥1.00.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00. A lowercase "ns" denotes relative risk less than 1.00.

12.5 CONCLUSION

Five psychological disorders, which were verified by a medical records review, and 12 measures from the SCL-90-R inventory were examined in the psychology assessment. The SCL-90-R consisted of nine primary symptom dimensions and three broad indices of psychological distress. In enlisted groundcrew, a significantly greater percentage of Ranch Hands than Comparisons had a history of other neuroses for both the unadjusted analyses and the analyses adjusted for covariates. All other adjusted analyses of Ranch Hands versus Comparisons that were significant showed a greater percentage of Comparisons than Ranch Hands with high SCL-90-R scores.

Associations between initial dioxin and the psychological endpoints in the analyses adjusted for covariates were either nonsignificant or revealed a significant decrease in high SCL-90-R scores as initial dioxin increased.

Differences in the history of psychological disorders and the prevalence of high SCL-90-R scores were examined between Comparisons and Ranch Hands categorized by dioxin levels. Ranch Hands in the low dioxin category and the low and high dioxin categories combined displayed a significantly higher prevalence of other neuroses than Comparisons in both the unadjusted and adjusted analyses.

The relation between the 1987 dioxin levels and the psychological endpoints was examined; all results were nonsignificant.

In conclusion, Ranch Hand veterans exhibited a significantly increased prevalence of other neuroses among enlisted groundcrew, the occupation with the highest dioxin levels and, presumably, the greatest herbicide exposure. Consistent increases in the prevalence of other neuroses with dioxin levels were found. No consistent relation was found between any SCL-90-R score and any measure of herbicide or dioxin exposure. The relation between other neuroses and herbicide exposure and dioxin levels will be described in greater detail in a separate report.

REFERENCES

1. Peterson, R. E., M. D. Seefeld, B. J. Christian, C. L. Potter, C. K. Kelling, and R. E. Keesey. 1984. The wasting syndrome in 2,3,7,8-tetrachlorodibenzo-p-dioxin toxicity: Basic features and their interpretation. In *Banbury Report 18: Biological mechanisms of dioxin action.* Eds. A. Poland and R. D. Kimbrough. Cold Spring Harbor, New York: Cold Spring Harbor Laboratory.

2. Piper, W. N., J. Q. Rose, and P. J. Gehring. 1973a. Excretion and tissue distribution of 2,3,7,8-tetrachlorodibenzo-p-dioxin in the rat. *Environmental Health Perspectives* 5:241-4.

3. Gasiewicz, T. A., L. E. Geiger, G. Rucci, and R. A. Neal. 1983. Distribution, excretion, and metabolism of 2,3,7,8-tetrachlordibenzo-p-dioxin in C57BL/6J, DBA/2J, and B6D2F1/J mice. *Drug Metabolism and Disposition* 11:397-403.

4. Abraham, K., T. Weismüller, H. Hagenmaier, and D. Neubert. 1990. Distribution of PCDDs and PCDFs in various tissues of marmoset monkeys. *Chemosphere* 20:1071-8.

5. Sirkka, U., S. A. Nieminen, R. Pohjanvirta, J. Tuomisto, and P. Ylitalo. 1990. Behavioral effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in rats. *European Journal of Pharmacology* 183:1517.

6. Sirkka, U., R. Pohjanvirta, S. A. Nieminen, J. Tuomisto, and P. Ylitalo. 1992. Acute neurobehavioral effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in rats. *Pharmacology and Toxicology* 71:284-8.

7. Bowman, R. E., S. L. Schantz, M. L. Gross, and S. A. Ferguson. 1989. Behavioral effects in monkeys exposed to 2,3,7,8-TCDD transmitted maternally during gestation and for four months of nursing. *Chemosphere* 18:235-42.

8. Bowman, R. E., S. L. Schantz, and S. A. Ferguson. 1990. Controlled exposure of female rhesus monkeys to 2,3,7,8-TCDD: Cognitive behavioral effects in their offspring. *Chemosphere* 20:1103-8.

9. Schantz, S. L., and R. E. Bowman. 1989. Learning in monkeys exposed perinatally to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Neurotoxicology and Teratology* 11:13-9.

10. Schantz, S., S. Ferguson, and R. Bowman. 1992. Effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin on behavior of monkeys in peer groups. *Neurotoxicology and Teratology* 14(6):433-46.

11. Ashe, W. F., and R. R. Suskind. 1949, 1950. Reports on chloracne cases. In Report of the Kettering Laboratory. Nitro, West Virginia: Monsanto Chemical Company.

12. Suskind, R. R. 1953. A clinical and environmental survey. In Report of the Kettering Laboratory. Nitro, West Virginia: Monsanto Chemical Company.

13. Moses, M., R. Lilis, K. D. Crow, J. Thornton, A. Fischbein, H. A. Anderson, and I. J. Selikoff. 1984. Health status of workers with past exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin in the manufacture of 2,4,5-trichlorophenoxyacetic acid: Comparison of findings with and without chloracne. *American Journal of Industrial Medicine* 5:161-82.

14. Suskind, R. R., and V. S. Hertzberg. 1984. Human health effects of 2,4,5-T and its toxic contaminants. *Journal of the American Medical Association* 251:2372-80.

15. Baader, E. W., and A. J. Bauer. 1951. Industrial intoxication due to pentachlorophenol. *Industrial Medicine and Surgery* 20:289-90.

16. Suskind, R. R. 1977. Chloracne and associated health problems in the manufacture of 2,4,5-T. Report to the Joint Conference, National Institute of Environmental Health Sciences and International Agency for Research on Cancer, World Health Organization, January, at Lyon, France.

17. Vos, J. G., T. J. Sterringa, D. Zellenrath, H. J. Docter, and L. M. Daldkerup. 1977. TCDD accident at a chemical factory in the Netherlands. Report to the Joint Conference, National Institute of Environmental Health Sciences and International Agency for Research on Cancer, World Health Organization, January, at Lyon, France.

18. Pazderova-Vejlupkova, J., M. Nemcova, J. Pickova, L. Jirasek, and E. Lukas. 1981. The development and prognosis of chronic intoxication by tetrachlorodibenzo-p-dioxin in men. *Archives of Environmental Health* 36:5-11.

19. Poland, A. P., D. Smith, G. Metter, and P. Possick. 1971. A health survey of workers in a 2,4-D and 2,4,5-T plant, with special attention to chloracne, porphyria cutanea tarda, and psychologic parameters. *Archives of Environmental Health* 22:316-27.

20. Oliver, R. M. 1975. Toxic effects of 2,3,7,8-tetrachlorodibenzo-1,4-dioxin in laboratory workers. *British Journal of Industrial Medicine* 32:46-53.

21. Hoffman, R. E., P. A. Stehr-Green, K. B. Webb, G. Evans, A. P. Knutsen, W. F. Schramm, J. L. Staake, B. B. Gibson, and K. K. Steinberg. 1986. Health effects of long-term exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Journal of the American Medical Association* 225:2031-8.

22. Stehr-Green, P. A., R. Hoffman, K. Webb, R. G. Evans, A. Knutsen, W. Schramm, J. Staake, B. Gibson, and K. Steinberg. 1987. Health effects of long-term exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Chemosphere* 16:2089-94.

23. Alderfer, R., M. Sweeney, M. Fingerhut, R. Hornung, K. Wille, and A. Fidler. 1992. Measures of depressed mood in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Chemosphere* 25(1-2):247-50.

24. Robinowitz, R., W. R. Roberts, M. P. Dolan, E. T. Patterson, H. L. Charles, H. G. Atkins, and W. E. Penk. 1989. Carcinogenicity and teratogenicity vs. psychogenicity: Psychological characteristics associated with self-reported Agent Orange exposure among Vietnam combat veterans who seek treatment for substance abuse. *Journal of Clinical Psychology* 45:718-28.

25. Decoufle, P., P. Holmgreen, C. A. Boyle, and N. E. Stroup. 1992. Self-reported health status of Vietnam veterans in relation to perceived exposure to herbicides and combat. *American Journal of Epidemiology* 135:312-23.

26. Stellman, J. D., S. D. Stellman, and J. F. Sommer Jr. 1988. Social and behavioral consequences of the Vietnam experience among American Legionnaires. *Environmental Research* 47:129-49.

27. U. S. Centers for Disease Control. 1988. Health status of Vietnam veterans. In part 1, Psychosocial characteristics. *Journal of the American Medical Association* 259:2701-2.

28. Lathrop, G. D., W. H. Wolfe, R. A. Albanese, and P. M. Moynahan. 1984. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Baseline Morbidity Study Results. NTIS: AD A 138-340. United States Air Force School of Aerospace Medicine, Brooks Air Force Base, Texas.

29. Lathrop, G. D., S. G. Machado, T. G. Karrison, W. D. Grubbs, W. F. Thomas, W. H. Wolfe, J. E. Michalek, J. C. Miner, and M. R. Peterson. 1987. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: First followup examination results. NTIS: AD A 188262. United States Air Force School of Aerospace Medicine, Brooks Air Force Base, Texas.

30. Thomas, W. F., W. D. Grubbs, T. G. Karrison, M. B. Lustik, R. H. Roegner, D. E. Williams, W. H. Wolfe, J. E. Michalek, J. C. Miner, and R. W. Ogershok. 1990. An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: I. 1987 followup examination results, May 1987 to January 1990. NTIS: AD A 222 573. United States Air Force School of Aerospace Medicine, Human Systems Division (AFSC), Brooks Air Force Base, Texas.

31. Derogatis, L. R. 1975. *The SCL-90-R.* Baltimore, Maryland: Clinical Psychometrics Research.

32. Michalek, J. E., J. L. Pirkle, S. P. Caudill, R. C. Tripathi, D. G. Patterson Jr., and L. L. Needham. 1996. Pharmacokinetics of TCDD in Veterans of Operation Ranch Hand: 10-year Followup. *Journal of Toxicology and Environmental Health* 47:209-20.

33. Institute of Medicine. 1994. *Veterans and Agent Orange: Health Effects of Herbicides Used in Vietnam.* National Academy Press: Washington, DC.

34. Institute of Medicine. 1996. *Veterans and Agent Orange: Update 1996.* National Academy Press: Washington, DC.

AIR FORCE HEALTH STUDY

FINAL REPORT

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Health Effects in Air Force Personnel
Following Exposure to Herbicides

VOLUME II

1997 Follow-up Examination Results
May 1997 to February 2000

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Volume II

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List of Tables

TABLE OF CONTENTS-REPORT

Table of Contents

List of Tables

13 GASTROINTESTINAL ASSESSMENT

13.1 INTRODUCTION

13.1.1 Background

In contrast with the wealth of dioxin research data available in animal models, there is relatively little information about the effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (dioxin) on the human digestive system. Although the pharmacokinetics of orally ingested dioxin in a human volunteer have been reported (1), the pathologic lesions that have been studied in animals (gastric metaplasia with ulceration and ileitis) have not been described in human populations, in which the principal route of exposure has been transcutaneous. Further, in two reports of extreme phenoxyherbicide toxicity by ingestion in three humans, the primary target organs were the central nervous system with associated coma and the musculoskeletal system with rhabdomyolysis and renal failure, rather than the digestive system (2, 3).

The digestive system and, particularly, the liver (4–9) and stomach (5, 10–14) have been clearly defined as target organs for dioxin toxicity in numerous laboratory animals. Dioxin ingested by rodents (15–20) and adult monkeys (21) is absorbed by the intestinal lymphatics, transported by chylomicrons in the enterohepatic, and preferentially stored in adipose tissue and the liver. Hepatotoxic manifestations, which appear to be dose- and time-dependent, include cellular hypertrophy, parenchymal necrosis (principally centrilobular), fatty degeneration, and the production of altered hepatic foci, a microscopic precursor in hepatic carcinogenesis (9, 22–24). Chronic feeding studies have confirmed the role of dioxin as a hepatic carcinogen in rats (25, 26) and mice (27). Gastric endpoints have been the subject of several reports that have focused on histologic changes (5, 12, 13) and endocrine secretory abnormalities (10, 11, 28) associated with dioxin toxicity.

A host of hepatic biochemical reactions related to dioxin toxicity has been studied, including lipid peroxidation (29–33), hepatic prostaglandin synthetase activity (34), and inhibition of glutathione peroxidase (30). Results from several lines of biochemical investigation have created a bridge between animal and human studies including research into lipid (33, 35–37) and porphyrin metabolism (38–41). In rats, dioxin has been shown to increase the activity of glucuronyl transferase (42), an observation that led to the use of urinary d-glucaric acid as a marker for dioxin exposure in several human epidemiological studies (43–47). The most recent of these, and the only one to include serum dioxin levels, found no correlation between this index and the body burden of dioxin (47).

In published occupational and environmental studies, acid peptic disease is the only digestive disorder intrinsic to the gastrointestinal tract that has been examined in relation to dioxin exposure. The finding of an increased cumulative incidence of ulcer disease reported in two studies (48, 49) was not confirmed in others (47, 50). In the only occupational study to include serum dioxin levels, the cumulative incidence of gastritis, ulcer disease, and gastrointestinal hemorrhage was similar in exposed workers (mean serum dioxin of 220 picograms [pg] per gram of lipid) and controls (mean of 7 pg per gram of lipid) (47).

Numerous occupational and environmental studies have reported abnormally elevated liver enzymes in association with exposure to dioxin, although in most cases there was no other clinical evidence for underlying liver disease (47–54). In longer-term follow-up studies, abnormalities noted at the time of acute exposure resolved over time (46, 54–57). In two environmental contamination studies conducted in 1984-85 at Quail Run (46) and in 1983 at Times Beach (58), Missouri, there was no evidence for hepatic

enzyme elevations in association with exposure to dioxin. In the 1987-88 National Institute of Occupational Safety and Health study (47), the prevalence of an abnormally elevated liver enzyme gamma glutamyl transferase (GGT) was significantly higher in the exposed cohort, but the association was noted only in those with significant alcohol consumption and did not appear directly related to the body burden of dioxin. Three recently published occupational studies found no significant association between elevated hepatic enzymes and serum dioxin levels (59–61).

Several reports of Vietnam veterans have focused on the potential association of hepatic disease with herbicide exposure. In one retrospective cohort study, in which the self-reporting of a rash during or after duty in Vietnam was used as a surrogate for dioxin exposure, an increased prevalence of liver enzyme abnormalities was noted but was attributed to prior viral hepatitis and alcohol consumption (62). Similarly, chronic alcoholism contributed to increased mortality from digestive diseases (cirrhosis and peptic ulcer) in a study of United States Army Chemical Corps veterans (63). Finally, in the most recent reports of the Air Force Health Study (AFHS), which have included serum dioxin levels in the analyses, there has been no increase in the prevalence of biologically meaningful hepatic or digestive disease in the Ranch Hand versus the Comparison cohorts (64, 65), although GGT and alanine aminotransferase (ALT) have been found to increase with dioxin body burden in Ranch Hand veterans. For example, GGT was significantly increased in the high dioxin category at the 1992 follow-up examination.

13.1.2 Summary of Previous Analyses of the Air Force Health Study

13.1.2.1 1982 Baseline Study Summary Results

The 1982 AFHS examination included an extensive evaluation of hepatic status by questionnaire, physical examination, and laboratory testing. The questionnaire elicited data on liver conditions, liver disease, and symptoms compatible with porphyria cutanea tarda (PCT), as well as detailed information on PCT risk factors (e.g., alcohol consumption, chemical exposures). The physical examination measured hepatomegaly, or enlarged liver, when present and determined liver function and porphyrin patterns by a comprehensive battery of 12 laboratory tests.

The questionnaire showed that Ranch Hands reported more miscellaneous liver conditions (verified by a medical records review) and more skin changes compatible with PCT than their Comparisons. Although the reported skin changes were statistically significant, no cases of PCT were diagnosed at examination in either cohort.

Ranch Hands had significantly higher GGT and lactic dehydrogenase (LDH) means and lower cholesterol means; no differences were found for bilirubin or alkaline phosphatase means. There were no significant group differences in uroporphyrin, coproporphyrin, or d-aminolevulinic acid levels, nor did any test set support a diagnosis of PCT.

A comprehensive hepatic evaluation did not reveal any consistent pattern of significant liver damage in the Ranch Hand group.

13.1.2.2 1985 Follow-up Study Summary Results

The 1985 AFHS examination continued the emphasis on hepatic function and expanded the porphyrin test battery to six assays. The interval questionnaire revealed sparse reporting of liver disorders from 1982 to 1985. Reported liver diseases were verified by medical records, and these data were added to the verified baseline history to assess possible lifetime differences. No significant differences were found.

The physical examination disclosed a marginally significant increase of hepatomegaly in the Ranch Hand group. Emphasis was placed on nine laboratory test variables measuring liver functions: aspartate aminotransferase (AST), ALT, GGT, alkaline phosphatase, total and direct bilirubin, LDH, cholesterol, and triglycerides. In addition, uroporphyrin and coproporphyrin measurements were obtained to assess the likelihood of PCT.

Only four variables produced differences of any note. The results showed a significantly lower mean ALT level, a greater mean alkaline phosphatase level, a lower mean uroporphyrin level, and a marginally significant greater mean coproporphyrin level in Ranch Hands. The risk of alkaline phosphatase abnormality was marginally significantly increased in Ranch Hands.

Overall, the 1985 follow-up examination laboratory data showed no adverse clinical or exposure patterns. The continuous statistical tests detected significant mean shifts that were not mirrored by the discrete tests. These findings were generally consistent with the 1982 baseline examination data. Slight differences in analytic results probably were due to the use of more fully adjusted models for the 1985 follow-up examination data.

Interval reporting of PCT-like symptoms of skin patches, bruises, and sensitivity was significantly increased in Ranch Hands. When these historic data were contrasted to both uroporphyrin and coproporphyrin abnormalities, no correlation was apparent, nor were there any significant group differences. The likelihood of bona fide PCT among Ranch Hands appeared to be remote.

13.1.2.3 1987 Follow-up Study Summary Results

Overall, the gastrointestinal assessment did not find the health of the Ranch Hand group to be significantly different from that of the Comparison group. Group differences based on verified historical data from the questionnaire were not significant for eight categories of liver disease. No significant group difference was found for past or present occurrence of peptic ulcers. The prevalence of hepatomegaly diagnosed at the physical examination also was not significantly different between the two groups. The only significant finding from the laboratory examination variables was that Ranch Hands had a higher mean alkaline phosphatase than Comparisons, also noted at the 1985 follow-up examination. Group differences for the other laboratory variables (AST, ALT, GGT, total bilirubin, direct bilirubin, LDH, cholesterol, high-density lipoprotein [HDL], cholesterol-HDL ratio, triglycerides, and creatine phosphokinase) were not significant.

13.1.2.4 Serum Dioxin Analysis of 1987 Follow-up Study Summary Results

The 1987 serum dioxin analyses did not show a significant association with any of the verified historical liver disorder variables. The analyses of the laboratory variables detected significant associations between dioxin (current and estimated initial) and lipid-related health indices such as cholesterol, HDL cholesterol, the cholesterol-HDL ratio, and triglycerides. These findings were consistent with significant associations seen for fat-related variables in other clinical assessments, such as the body fat results in the general health assessment and the diabetes and glucose results noted in the endocrine assessment, and may represent a dioxin mediated alteration of biochemical processes.

13.1.2.5 1992 Follow-up Study Summary Results

The gastrointestinal assessment found isolated significant differences between Ranch Hands and Comparisons, but overall, the health of the two groups did not differ substantially. The serum dioxin analyses indicated that estimated initial dioxin generally was not associated with historical liver disorders

or current laboratory measurements. The analyses did reveal that current dioxin levels were often highly associated with lipid-related health indices, such as cholesterol, HDL cholesterol, the cholesterol-HDL ratio, and triglycerides, as well as with some of the hepatic enzymes (ALT and GGT) and proteins. These seemingly discordant results may have been explained in part because the initial dioxin analyses adjusted for differential half-life elimination related to body fat, while no adjustment was made in the analyses of current dioxin. These significant findings may have been the result of a subclinical dioxin effect on lipid metabolism.

13.1.3 Parameters for the 1997 Gastrointestinal Assessment

13.1.3.1 Dependent Variables

Questionnaire, physical examination, and laboratory data were used in the gastrointestinal assessment. The questionnaire data were organized by International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) medical coding categories.

13.1.3.1.1 Medical Records Data

During the 1997 health interview, each study participant was asked about the occurrence of hepatitis, jaundice, cirrhosis, enlarged liver, and other liver conditions. This self-reported information was elicited in the questionnaire and combined with information from the baseline, 1985, 1987, and 1992 follow-up examinations and verified by a medical records review. The verified results were grouped into eight categories of disorders for analysis: uncharacterized hepatitis (non-A, non-B, non-C, and non-D), jaundice (unspecified, not of the newborn), acute necrosis of the liver, chronic liver disease and cirrhosis (alcohol-related and non-alcohol-related cirrhosis were analyzed separately), liver abscess and sequelae of chronic liver disease, enlarged liver (hepatomegaly), and other disorders of the liver. The purpose of the uncharacterized hepatitis (non-A, non-B, non-C, and non-D) category was to define a category that was neither clearly A nor B nor C nor D, so that liver disease misdiagnosed as "viral hepatitis" could be detected. This approach to historical hepatitis created a group of cases that could have been chemically induced. The following ICD-9-CM codes were used for these disorders: uncharacterized hepatitis (ICD-9-CM codes 070.49, 070.59, 070.6, 070.9, 571.40, 571.41, 571.49, and 573.3), jaundice (ICD-9-CM code 782.4), acute necrosis of the liver (ICD-9-CM code 570), alcohol-related chronic liver disease and cirrhosis (ICD-9-CM codes 571.0–571.3), non-alcohol-related chronic liver disease and cirrhosis (ICD-9-CM codes 571.40–571.9), liver abscess and sequelae of chronic liver disease (ICD-9-CM codes 572.0–572.4, 572.8), enlarged liver (ICD-9-CM code 789.1), and other disorders of the liver (ICD-9-CM codes 573.0–573.9, 790.4, 790.5, and 794.8).

For each condition, participants with a pre-Southeast Asia (SEA) diagnosis were excluded from the analysis. Also, the analysis of alcohol-related chronic liver disease and cirrhosis excluded participants with zero lifetime alcohol history because nondrinkers were not at risk for alcohol-related liver disease.

13.1.3.1.2 Physical Examination Data

One variable from the 1997 physical examination, current hepatomegaly, was analyzed in the gastrointestinal assessment. This variable was coded as "yes" or "no." Participants whose blood contained hepatitis B surface antigen or hepatitis C antibodies were excluded from the analysis of current hepatomegaly to account for the effects of these viruses on chronic hepatic disease.

13.1.3.1.3 *Laboratory Examination Data*

The 1997 examination emphasized the evaluation of laboratory data through the analysis of 29 measurements. These laboratory variables were AST (U/l), ALT (U/l), GGT (U/l), alkaline phosphatase (U/l), total bilirubin (mg/dl), direct bilirubin (mg/dl), LDH (U/l), cholesterol (mg/dl), HDL (mg/dl), cholesterol-HDL ratio, triglycerides (mg/dl), creatine phosphokinase (U/l), serum amylase (U/l), antibodies for hepatitis A, serological evidence of prior hepatitis B infection (positive hepatitis B core antibody), current hepatitis B (positive hepatitis B surface antigen), antibodies for hepatitis C, antibodies for hepatitis D, stool hemoccult, and 10 components (in mg/dl) in a protein profile (prealbumin, albumin, α-1-acid glycoprotein, α-1-antitrypsin, α-2-macroglobulin, apolipoprotein B, C3 complement, C4 complement, haptoglobin, and transferrin). IgA, IgG, and IgM were also part of this profile, but they were analyzed in the immunologic assessment (see Chapter 17).

All assays for the 1997 gastrointestinal assessment were performed by Scripps Clinic. Dade RxL® equipment was used to quantify AST, ALT, GGT, alkaline phosphatase, total bilirubin, direct bilirubin, LDH, cholesterol, HDL, triglycerides, creatine phosphokinase, serum amylase, and albumin. The Beckman Array Protein System® quantified all components of the protein profile except albumin.

Abbott Commander® equipment was used to determine the presence or absence of antibodies of hepatitis A, serological evidence of prior hepatitis B infection, current hepatitis B, and antibodies of hepatitis C. Abbott Quantum® equipment was used to determine the presence or absence of hepatitis D antibodies. Hepatitis D testing was performed only on participants who showed serological evidence of prior hepatitis B infection or current hepatitis B, as determined by a positive hepatitis B surface antigen.

All laboratory variables were analyzed in both continuous and discrete forms except for direct bilirubin, antibodies for hepatitis A, serological evidence of present or prior hepatitis B infection, current hepatitis B, antibodies for hepatitis C, antibodies for hepatitis D, and stool hemoccult, which were analyzed only in discrete form. Direct bilirubin was analyzed only in its discrete form because there were few distinct measurements, precluding a meaningful continuous analysis.

Participants whose blood contained hepatitis B surface antigen, hepatitis C antibodies, or hepatitis D antibodies were excluded from the analysis of all laboratory variables except antibodies for hepatitis A, serological evidence of prior hepatitis B infection, current hepatitis B, antibodies for hepatitis C, and antibodies for hepatitis D. Participants with body temperatures greater than or equal to 100° Fahrenheit also were excluded from the analysis of these variables. For the five hepatitis variables, no participants were excluded. Attempts were made to determine, from a medical records review, which occurrences of the types of hepatitis described above were pre-SEA, but the date of hepatitis onset was not available for the majority of participants. Consequently, all occurrences of hepatitis are included in these variables.

13.1.3.2 *Covariates*

Statistical analyses of all medical records variables were adjusted for age, race, military occupation, lifetime alcohol history, lifetime industrial chemical exposure, and lifetime degreasing chemical exposure.

Statistical analyses of the physical examination variable and all of the laboratory variables except alkaline phosphatase and α-1-antitrypsin were adjusted for age, race, military occupation, current alcohol use, lifetime alcohol history, lifetime industrial chemical exposure, and lifetime industrial chemical exposure. Wine consumption showed a strong negative association with alkaline phosphatase in the 1985, 1987, and 1992 follow-up examinations. The negative association persisted in the 1992 and 1997 follow-up examination data; therefore, current wine consumption and lifetime wine history replaced current alcohol use and lifetime alcohol history as covariates in the adjusted analyses of alkaline phosphatase. Current

wine consumption also replaced current alcohol use in the adjusted analysis of α-1-antitrypsin based on covariate associations in the 1997 follow-up examination data, which showed that α-1-antitrypsin was highly associated with current wine consumption but not associated with current alcohol use.

Age, race, and military occupation were determined from military records. Lifetime alcohol (or wine) history was based on information from the 1997 questionnaire and combined with similar information gathered at the 1987 and 1992 follow-up examinations. Each participant was asked about his drinking patterns throughout his lifetime. When a participant's drinking patterns changed, he was asked to describe how his alcohol consumption differed and the duration of time that the drinking pattern lasted. The participant's average daily alcohol consumption was determined for each of the reported drinking pattern periods throughout his lifetime, and an estimate of the corresponding total number of drink-years was derived. One drink-year was the equivalent of drinking 1.5 ounces of an 80-proof alcoholic beverage, one 12-ounce beer, or one 5-ounce glass of wine per day for 1 year. Current alcohol use (or wine consumption) was based on the average number of drinks per day during the month prior to completing the questionnaire.

The participants' lifetime exposures through 1992 to degreasing and industrial chemicals were updated with information reported in the 1997 questionnaire.

Age, current alcohol use (or wine consumption), and lifetime alcohol (or wine) history were treated as continuous variables wherever possible for all adjusted analyses. Degreasing chemical exposure and industrial chemical exposure were categorized as "yes" or "no" for all analyses.

13.1.4 Statistical Methods

Table 13-1 summarizes the statistical analysis performed for the gastrointestinal assessment. The first part of this table lists the dependent variables analyzed, source of the data, form of the data (discrete or continuous), cutpoints, covariates, and statistical methods. The second part of this table provides a further description of the covariates examined. A covariate was used in its continuous form whenever possible for all adjusted analyses; if the covariate was inherently discrete (e.g., military occupation), or if a categorized form was needed to develop measures of association with the dependent variables, the covariate was categorized as shown in Table 13-1.

Cutpoints for cholesterol are age-dependent. Consequently, normal and abnormal levels were constructed according to a participant's laboratory value and age at the physical examination. The age-specific cutpoints are listed in Table 13-1, and the reference ages for these cutpoints are given in parentheses following the cutpoints.

Table 13-1. Statistical Analysis for the Gastrointestinal Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
Uncharacterized Hepatitis	MR-V	D	Yes No	(1)	(a)	U:LR A:LR
Jaundice (Unspecified)	MR-V	D	Yes No	(1)	(a)	U:LR,CS A:LR

Table 13-1. Statistical Analysis for the Gastrointestinal Assessment (Continued)

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
Acute Necrosis of the Liver	MR-V	D	Yes No	(1)	(a)	--
Chronic Liver Disease and Cirrhosis (Alcohol-related)	MR-V	D	Yes No	(1)	(b)	U:LR A:LR
Chronic Liver Disease and Cirrhosis (Non-alcohol-related)	MR-V	D	Yes No	(1)	(a)	U:LR A:LR
Liver Abscess and Sequelae of Chronic Liver Disease	MR-V	D	Yes No	(1)	(a)	U:LR,CS A:LR
Enlarged Liver (Hepatomegaly)	MR-V	D	Yes No	(1)	(a)	U:LR A:LR
Other Disorders of the Liver	MR-V	D	Yes No	(1)	(a)	U:LR A:LR
Current Hepatomegaly	PE	D	Yes No	(2)	(c)	U:LR,CS A:LR
AST (U/l)	LAB	D/C	High: >37 Normal: ≤37	(2)	(d)	U:LR,GLM A:LR,GLM L:LR,GLM
ALT (U/l)	LAB	D/C	High: >65 Normal: ≤65	(2)	(d)	U:LR,GLM A:LR,GLM L:LR,GLM
GGT (U/l)	LAB	D/C	High: >85 Normal: ≤85	(2)	(d)	U:LR,GLM A:LR,GLM L:LR,GLM
Alkaline Phosphatase (U/l)	LAB	D/C	High: >136 Normal: ≤136	(3)	(d)	U:LR,GLM A:LR,GLM
Total Bilirubin (mg/dl)	LAB	D/C	High: >1.0 Normal: ≤1.0	(2)	(d)	U:LR,GLM A:LR,GLM
Direct Bilirubin (mg/dl)	LAB	D	High: >0.3 Normal: ≤0.3	(2)	(d)	U:LR,CS A:LR
Lactic Dehydrogenase (LDH) (U/l)	LAB	D/C	High: >190 Normal: ≤190	(2)	(d)	U:LR,GLM A:LR,GLM
Cholesterol (mg/dl)	LAB	D/C	High: >260 (Age 45–49) >250 (Age ≥50) Normal: ≤260 (Age 45–49) ≤250 (Age ≥50)	(2)	(d)	U:LR,GLM A:LR,GLM L:LR,GLM
HDL Cholesterol (mg/dl)	LAB	D/C	Low: <32 Normal: ≥32	(2)	(d)	U:LR,GLM A:LR,GLM L:LR,GLM
Cholesterol-HDL Ratio	LAB	D/C	High: >5 Normal: ≤5	(2)	(d)	U:LR,GLM A:LR,GLM L:LR,GLM

Table 13-1. Statistical Analysis for the Gastrointestinal Assessment (Continued)

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
Triglycerides (mg/dl)	LAB	D/C	High: >200 Normal: ≤200	(2)	(d)	U:LR,GLM A:LR,GLM L:LR,GLM
Creatine Phosphokinase (U/l)	LAB	D/C	High: >232 Normal: ≤232	(2)	(d)	U:LR,GLM A:LR,GLM
Serum Amylase (U/l)	LAB	D/C	High: >115 Normal: ≤115	(2)	(d)	U:LR,GLM A:LR,GLM
Antibodies for Hepatitis A	LAB	D	Yes No	(2)	None	U:LR A:LR
Serological Evidence of Prior Hepatitis B Infection	LAB	D	Yes No	(2)	(e)	U:LR A:LR
Current Hepatitis B	LAB	D	Yes No	(2)	None	U:LR,CS A:LR
Antibodies for Hepatitis C	LAB	D	Yes No	(2)	None	U:LR A:LR
Antibodies for Hepatitis D	LAB	D	Yes No	(2)	None	--
Stool Hemoccult	LAB	D	Yes No	(2)	(d)	U:LR A:LR
Protein Profile: Prealbumin (mg/dl)	LAB	D/C	Low: <18 Normal: ≥18	(2)	(d)	U:LR,GLM A:LR,GLM
Protein Profile: Albumin (mg/dl)	LAB	D/C	Low: <3,350 Normal: ≥3,350	(2)	(d)	U:LR,CS,GLM A:LR,GLM
Protein Profile: α-1-Acid Glycoprotein (mg/dl)	LAB	D/C	High: >125 Normal: ≤125	(2)	(d)	U:LR,GLM A:LR,GLM
Protein Profile: α-1-Antitrypsin (mg/dl)	LAB	D/C	Abnormal Low: <93 Normal: 93-224 Abnormal High: >224	(4)	(d)	U:PR,CS,GLM A:PR,GLM
Protein Profile: α-2-Macroglobulin (mg/dl)	LAB	D/C	High: >293 Normal: ≤293	(2)	(d)	U:LR,GLM A:LR,GLM
Protein Profile: Apolipoprotein B (mg/dl)	LAB	D/C	High: >109 Normal: ≤109	(2)	(d)	U:LR,GLM A:LR,GLM
Protein Profile: C3 Complement (mg/dl)	LAB	D/C	Low: <85 Normal: ≥85	(2)	(d)	U:LR,GLM A:LR,GLM
Protein Profile: C4 Complement (mg/dl)	LAB	D/C	Low: <12 Normal: ≥12	(2)	(d)	U:LR,CS,GLM A:LR,GLM
Protein Profile: Haptoglobin (mg/dl)	LAB	D/C	High: >163 Normal: ≤163	(2)	(d)	U:LR,GLM A:LR,GLM
Protein Profile: Transferrin (mg/dl)	LAB	D/C	Low: <212 Normal: ≥212	(2)	(d)	U:LR,GLM A:LR,GLM

Table 13-1. Statistical Analysis for the Gastrointestinal Assessment (Continued)

[a]Covariates:
(1): age, race, military occupation, lifetime alcohol history, industrial chemical exposure, degreasing chemical exposure.
(2): age, race, military occupation, current alcohol use, lifetime alcohol history, industrial chemical exposure, degreasing chemical exposure.
(3): age, race, military occupation, current wine consumption, lifetime wine history, industrial chemical exposure, degreasing chemical exposure.
(4): age, race, military occupation, current wine consumption, lifetime alcohol history, industrial chemical exposure, degreasing chemical exposure.

[b]Exclusions:
(a): participants with a pre-SEA history of the disorder.
(b): participants with a pre-SEA history of the disorder, participants with no lifetime alcohol history.
(c): participants whose blood contained hepatitis B surface antigen, hepatitis C antibodies, or hepatitis D antibodies.
(d): participants whose blood contained hepatitis B surface antigen, hepatitis C antibodies, or hepatitis D antibodies, participants with body temperatures greater than or equal to 100° Fahrenheit.
(e): participants who had received the hepatitis B vaccine.

Covariates

Variable (Units)	Data Source	Data Form	Cutpoints
Age (years)	MIL	D/C	Born ≥1942 Born <1942
Race	MIL	D	Black Non-Black
Occupation	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Current Alcohol Use (drinks/day)	Q-SR	D/C	0–1 >1–4 >4
Lifetime Alcohol History (drink-years)	Q-SR	D/C	0 >0–40 >40
Current Wine Consumption (drinks of wine/day)	Q-SR	D/C	0 >0
Lifetime Wine History (drink-years of wine)	Q-SR	D/C	0 >0
Industrial Chemical Exposure	Q-SR	D	Yes No
Degreasing Chemical Exposure	Q-SR	D	Yes No

Abbreviations

Data Source:
LAB: 1997 laboratory results
MIL: Air Force military records
MR-V: Medical records (verified)
PE: 1997 physical examination
Q-SR: Health questionnaires (self-reported)

Table 13-1. Statistical Analysis for the Gastrointestinal Assessment (Continued)

Data Form: D: Discrete analysis only
D/C: Discrete and continuous analysis for dependent variables; appropriate form for analysis (either discrete or continuous) for covariates

Statistical Analysis: U: Unadjusted analysis
A: Adjusted analysis
L: Longitudinal analysis

Statistical Methods: CS: Chi-square contingency table analysis (continuity-adjusted)
GLM: General linear models analysis
LR: Logistic regression analysis
PR: Polytomous logistic regression analysis

Table 13-2 provides a summary of the number of participants with missing dependent variable and covariate data. In addition, the number of participants excluded because of medical conditions is given.

Table 13-2. Number of Participants Excluded or with Missing Data for the Gastrointestinal Assessment

		Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
Variable	Variable Use	Ranch Hand	Comparison	Initial	1987	Ranch Hand	Comparison
Lactic Dehydrogenase	DEP	0	2	0	0	0	2
HDL	DEP	1	1	1	1	1	1
Cholesterol-HDL Ratio	DEP	1	1	1	1	1	1
Triglycerides	DEP	1	0	0	1	1	0
Antibodies for Hepatitis A	DEP	0	1	0	0	0	1
Serological Evidence of Prior Hepatitis B Infection	DEP	0	1	0	0	0	1
Stool Hemoccult	DEP	27	35	13	25	25	32
Current Alcohol Use	COV	1	0	0	1	1	0
Lifetime Alcohol History	COV	6	2	3	6	6	1
Current Wine Consumption	COV	1	0	0	1	1	0
Lifetime Wine History	COV	4	2	2	4	4	1
Pre-SEA Jaundice	EXC	24	32	13	24	24	31
Pre-SEA Chronic Liver Disease and Cirrhosis (Alcohol-related)	EXC	1	4	1	1	1	4
No Lifetime Alcohol History	EXC	54	64	34	54	54	62
Pre-SEA Chronic Liver Disease and Cirrhosis (Non-alcohol-related)	EXC	0	1	0	0	0	1
Pre-SEA Enlarged Liver	EXC	1	2	1	1	1	2
Pre-SEA Other Liver Disorders	EXC	4	11	1	4	4	11
Body Temperature ≥100° Fahrenheit at the Time of the Physical Exam	EXC	1	0	1	1	1	0
Hepatitis B Surface Antigen (Current Hepatitis B)	EXC	1	2	1	1	1	2

Table 13-2. Number of Participants Excluded or with Missing Data for the Gastrointestinal Assessment (Continued)

		Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
Variable	**Variable Use**	**Ranch Hand**	**Comparison**	**Initial**	**1987**	**Ranch Hand**	**Comparison**
Antibodies for Hepatitis C	EXC	9	18	4	9	9	17
Antibodies for Hepatitis D	EXC	1	0	1	1	1	0
Vaccinated for Hepatitis B	EXC	1	1	1	1	1	1

Note: DEP = Dependent variable.
COV = Covariate.
EXC = Exclusion.
870 Ranch Hands and 1,251 Comparisons.
482 Ranch Hands for initial dioxin; 863 Ranch Hands for 1987 dioxin.
863 Ranch Hands and 1,213 Comparisons for categorized dioxin.

13.1.4.1 Longitudinal Analysis

The longitudinal analysis of the gastrointestinal assessment examined seven laboratory variables (AST, ALT, GGT, cholesterol, HDL cholesterol, the cholesterol-HDL ratio, and triglycerides). Each variable was analyzed in both its continuous and discrete forms. These longitudinal analyses were used to assess any relation between herbicide exposure or dioxin levels and hepatic changes across time.

13.2 RESULTS

13.2.1 Dependent Variable-Covariate Associations

Covariate tests of association were performed to examine the relation between the covariates used in the adjusted analyses and the dependent variables. These associations are pairwise between the dependent variable and the covariate and are not adjusted for any other covariates. Appendix Table F-5 provides summary results of these analyses, including correlation coefficients (r), percents abnormal, means, and p-values to test the statistical significance of the associations. Statistically significant ($p \leq 0.05$) associations are discussed below.

13.2.1.1 Medical Records Variables

The association between a history of uncharacterized hepatitis and lifetime alcohol consumption was significant (p=0.010). Uncharacterized hepatitis decreased as lifetime alcohol consumption increased.

Tests of covariate association showed race (p=0.025), lifetime alcohol history (p=0.001), and industrial chemical exposure (p=0.024) to be significantly associated with alcohol-related chronic liver disease. Black participants had a higher prevalence of alcohol-related chronic liver disease than non-Blacks (9.5% vs. 4.5%). The percentage of participants with chronic liver disease increased as lifetime alcohol consumption increased. Participants who reported exposure to industrial chemicals had a higher percentage of alcohol-related chronic liver disease (5.6%) than participants who did not report exposure (3.3%).

Non-alcohol-related chronic liver disease was significantly associated with lifetime alcohol history (p=0.011). Moderate drinkers (in terms of drink-years) had the highest percentage of non-alcohol-related chronic liver disease (1.8%), followed by nondrinkers (1.7%) and heavier drinkers (0.2%).

The percentage of participants with enlarged livers increased with age (p=0.038) and lifetime alcohol history (p=0.001).

Other liver disorders were significantly associated with race (p=0.001) and lifetime alcohol history (p=0.043). The prevalence of other liver disorders was greater for Blacks (43.0%) than for non-Blacks (25.6%). The percentage of participants with a history of other liver disorders increased as drinking increased.

13.2.1.2 Laboratory Examination Variables

AST in its continuous form increased with current alcohol use (p<0.001) and lifetime alcohol history (p=0.002). Dichotomized AST showed an increase in the percentage of high AST levels as current alcohol use increased (p=0.001).

ALT in its discrete form was significantly associated with age (p<0.001) and occupation (p=0.009). Younger participants had a larger percentage of high ALT values than did older participants (10.0% vs. 5.4%). Enlisted flyers had the highest percentage of high ALT values (10.1%), followed by enlisted groundcrew (8.2%), then officers (5.4%). ALT in its continuous form significantly decreased with age (p<0.001) and increased with current alcohol use (p=0.009).

For GGT in its continuous form, tests of covariate association were significant for age (p<0.001), race (p=0.012), occupation (p=0.026), current alcohol use (p<0.001), and lifetime alcohol history (p<0.001). Levels of GGT decreased with age. Black participants showed significantly higher mean GGT levels than non-Blacks (48.65 U/l versus 42.70 U/l). Enlisted flyers had the highest mean GGT levels (44.91 U/l), followed by the enlisted groundcrew (43.87 U/l) and officers (41.38 U/l). GGT levels increased with current alcohol use and lifetime alcohol history. Tests of covariate association for GGT in its discrete form showed similar results, except that race was not significantly associated with the discrete form of GGT.

Alkaline phosphatase in its continuous form was significantly associated with occupation (p<0.001), current wine consumption (p<0.001), and lifetime wine history (p<0.001). Mean alkaline phosphatase levels decreased with current wine consumption and lifetime wine history. Enlisted flyers had the highest mean alkaline phosphatase level (83.60 U/l), followed by enlisted groundcrew (82.29 U/l) and officers (77.43 U/l).

Total bilirubin in its continuous form increased with age (p=0.005) and current alcohol use (p<0.001). Occupation (p=0.001) and degreasing chemical exposure (p=0.020) also were associated significantly with total bilirubin in its continuous form. Officers showed the highest mean total bilirubin level (0.544 mg/dl), followed by enlisted flyers (0.502 mg/dl) and enlisted groundcrew (0.504 mg/dl). Participants who reported exposure to degreasing chemicals had a higher mean total bilirubin level (0.536 mg/dl) than did those who did not report exposure (0.510 mg/dl). Results of the test for discretized total bilirubin revealed a significant association with current alcohol use (p=0.023). Participants who were currently moderate drinkers (in terms of drinks per day) had the lowest prevalence of high total bilirubin values (5.4%), followed by those who were lighter drinkers (5.7%) and those who were heavier drinkers (15.2%). The percentage of participants with high direct bilirubin levels increased with current alcohol use (p=0.004) and lifetime drinking history (p=0.013).

Lactic dehydrogenase in its continuous form increased with age (p<0.001).

Tests of covariate association for cholesterol in its continuous form showed a significant association with age (p=0.025), occupation (p=0.004), and current alcohol use (p<0.001). Cholesterol levels decreased with age and increased with current alcohol use. Enlisted flyers had the highest mean cholesterol levels (215.7 mg/dl), followed by the enlisted groundcrew (212.9 mg/dl) and officers (208.5 mg/dl).

Cholesterol in its discretized form showed significant associations with current alcohol use (p=0.009) and lifetime alcohol history (p=0.047). Participants who were moderate drinkers had the highest prevalence of high cholesterol levels (19.8%), followed by heavier drinkers (19.6%) and participants who were lighter drinkers (13.7%). The percentage of participants with high cholesterol levels increased with lifetime alcohol history.

HDL cholesterol in its continuous form increased with current alcohol use (p<0.001) and lifetime alcohol history (p<0.001). Race (p=0.002), occupation (p<0.001), industrial chemical exposure (p=0.005), and degreasing chemical exposure (p=0.001) also were associated significantly with HDL cholesterol. Black participants had higher mean HDL cholesterol levels than non-Blacks (48.17 mg/dl vs. 44.70 mg/dl). Officers had higher mean HDL cholesterol levels (46.67 mg/dl), followed by enlisted flyers (44.24 mg/dl) and enlisted groundcrew (43.59 mg/dl). Participants who reported exposure to industrial chemicals had lower mean HDL cholesterol levels (44.33 mg/dl) than those who did not report exposure (45.81 mg/dl). Similarly, participants who reported exposure to degreasing chemicals had lower mean HDL cholesterol levels (44.25 mg/dl) than those who did not report exposure (46.07 mg/dl).

Tests of covariate association for HDL cholesterol in its discrete form showed similar results. Significant covariates were occupation (p=0.002), current alcohol use (p=0.001), lifetime alcohol history (p=0.001), industrial chemical exposure (p=0.028), and degreasing chemical exposure (p=0.023). Race was not significantly associated with HDL cholesterol in its discrete form. Enlisted flyers had the highest percentage of low HDL cholesterol levels (10.2%), followed by the enlisted groundcrew (9.1%) and officers (5.2%). Participants who were currently light drinkers had the highest percentage of low HDL cholesterol levels (9.0%), followed by heavier drinkers (4.3%) and moderate drinkers (2.4%). The prevalence of low HDL cholesterol levels decreased as lifetime alcohol consumption increased. In each of the analyses of industrial chemical exposure and degreasing chemical exposure, participants who reported exposure had a higher percentage of low HDL cholesterol levels.

The cholesterol-HDL ratio in its continuous form decreased with age (p=0.003), current alcohol use (p<0.001), and lifetime alcohol history (p<0.001). Significant associations also were found with race (p=0.011), occupation (p<0.001), industrial chemical exposure (p<0.001), and degreasing chemical exposure (p<0.001). Non-Blacks had a higher mean cholesterol-HDL ratio than Blacks (4.69 vs. 4.39). Enlisted groundcrew had the highest mean cholesterol-HDL ratio (4.85), followed by enlisted flyers (4.84) and officers (4.43). For both industrial chemical exposure and degreasing chemical exposure covariates, participants who reported exposure had higher mean cholesterol-HDL ratios.

The tests of covariate association for the cholesterol-HDL ratio in its discrete form showed similar results. Younger participants had a higher prevalence of high cholesterol-HDL ratios than did the older participants (44.5% vs. 38.7%, p=0.008). Non-Blacks had a larger percentage of high cholesterol-HDL ratios than Blacks (42.0% vs. 28.3%, p=0.004). Occupation was significantly associated with the discrete form of the cholesterol-HDL ratio (p=0.001). Enlisted groundcrew had the highest prevalence of low cholesterol-HDL ratios (48.2%), followed by enlisted flyers (43.4%) and officers (32.6%). The percentage of participants with high cholesterol-HDL ratios decreased with increased current alcohol use (p=0.001) and increased lifetime alcohol history (p=0.001). For both industrial chemical exposure and degreasing chemical exposure covariates, participants who reported exposure had higher percentages of high cholesterol-HDL ratios (p=0.001 for both covariates).

Triglycerides in its continuous form significantly decreased with age ($p=0.001$). Significant associations with race ($p<0.001$), occupation ($p<0.001$), industrial chemical exposure ($p=0.013$), and degreasing chemical exposure ($p=0.002$) also were revealed. Non-Black participants had a higher mean triglycerides level than Blacks (123.5 mg/dl vs. 93.0 mg/dl). Enlisted flyers had the highest mean triglycerides level (131.3 mg/dl), followed by enlisted groundcrew (126.1 mg/dl) and officers (113.0 mg/dl). Participants who reported exposure to industrial chemicals had higher mean triglyceride levels than those who did not report exposure (124.9 mg/dl vs. 116.4 mg/dl). Similarly, participants who reported exposure to degreasing chemicals had higher mean triglyceride levels (125.6 mg/dl) than those who did not report exposure (114.7 mg/dl).

The tests of covariate association for triglycerides in its discrete form showed significant associations with age ($p=0.003$), race ($p=0.001$), occupation ($p=0.002$), industrial chemical exposure ($p=0.035$), and degreasing chemical exposure ($p=0.012$). The prevalence of high triglyceride levels was higher among the younger participants than the older participants (24.0% vs. 18.6%). Non-Blacks had a larger percentage of high triglycerides than Blacks (21.8% vs. 6.7%). Enlisted flyers had the highest percentage of high triglyceride levels (24.2%), followed by the enlisted groundcrew (23.2%) and officers (17.1%). For both industrial chemical exposure and degreasing chemical exposure covariates, participants who reported exposure had higher percentages of high triglyceride levels.

Creatine phosphokinase in its continuous form significantly decreased with age ($p<0.001$) and current alcohol use ($p=0.013$). Also significant were race ($p<0.001$) and occupation ($p=0.038$). Black participants had a higher mean creatine phosphokinase level than non-Blacks (195.9 U/l vs. 102.0 U/l). Enlisted groundcrew had the highest mean creatine phosphokinase levels (109.2 U/l), followed by officers (104.9 U/l), then enlisted flyers (99.2 U/l).

Tests of covariate association for creatine phosphokinase in its discrete form showed a significant association with age ($p=0.006$), race ($p=0.001$), and current alcohol use ($p=0.018$). Younger participants had a larger percentage of high creatine phosphokinase values than did the older participants (11.0% vs. 7.4%). Black participants had a larger percentage of high creatine phosphokinase values than non-Blacks (34.2% vs. 7.1%). Participants who were currently heavier drinkers had the highest prevalence of high creatine phosphokinase values (10.9%), followed by lighter drinkers (9.7%) and moderate drinkers (5.1%).

Serum amylase in its continuous form showed significant associations with race ($p<0.001$) and current alcohol use ($p=0.001$). Blacks had a higher mean serum amylase level (72.71 U/l) than non-Blacks (56.04 U/l). Serum amylase levels decreased as current alcohol use increased. The discrete form of serum amylase was significantly associated with race ($p=0.001$). Blacks had a larger percentage of high serum amylase values than non-Blacks (10.8% vs. 2.5%).

Tests of covariate association for the presence of antibodies for hepatitis A showed significant associations with age ($p=0.001$), race ($p=0.012$), occupation ($p=0.001$), and lifetime alcohol history ($p=0.001$). A higher percentage of the older participants had hepatitis A antibodies (40.9%) than the younger participants (23.5%). Black participants had a higher prevalence of hepatitis A antibodies than did non-Black participants (43.8% vs. 32.5%). Enlisted flyers had the highest percentage of participants with antibodies for hepatitis A (47.3%), followed by enlisted groundcrew (33.6%) and officers (27.0%). The highest percentage of positive results for hepatitis A antibodies was among nondrinkers (45.8%), followed by heavy lifetime drinkers (35.9%) and moderate lifetime drinkers (30.9%).

Evidence of prior hepatitis B infection was significantly associated with race ($p=0.001$), occupation ($p=0.001$), and lifetime alcohol history ($p=0.001$). Black participants had a higher percentage of prior hepatitis B infections than non-Blacks (26.8% vs. 10.7%). Enlisted flyers had the highest percentage of prior hepatitis B infections (16.6%), followed by enlisted groundcrew (14.9%) and officers (6.0%). The

percentage of participants with serological evidence of prior hepatitis B infections increased with lifetime alcohol consumption.

Current hepatitis B was significantly associated with race (p=0.001) and current alcohol use (p=0.002). Black participants had a higher percentage of positive current hepatitis B results than did non-Black participants (1.6% vs. 0.1%). Participants who were currently heavier drinkers had the highest prevalence of current hepatitis B (2.0%), followed by lighter drinkers (0.1%) and moderate drinkers (0.0%).

The presence of hepatitis C antibodies was significantly associated with race (p=0.002), occupation (p=0.024), current alcohol use (p=0.004), and industrial chemical exposure (p=0.022). Black participants had a higher percentage of positive hepatitis C results than non-Blacks (4.7% vs. 1.1%). Enlisted groundcrew had the highest prevalence of positive results for hepatitis C antibodies (2.0%), followed by enlisted flyers (0.9%) and officers (0.6%). Participants who were currently heavier drinkers had the highest percentage of positive hepatitis C results (6.0%), followed by lighter drinkers (1.2%) and moderate drinkers (0.5%). Participants who reported exposure to industrial chemicals had a higher percentage of positive hepatitis C results than did participants who did not report exposure (1.7% vs. 0.5%).

The results of the tests of covariate association for stool hemoccult revealed that age and industrial chemical exposure were statistically significant (p=0.006 and p=0.021, respectively). Older participants had a higher percentage of positive stool hemoccult results (5.1%) than did the younger participants (2.6%). Participants who did not report exposure to industrial chemicals had a higher prevalence of positive stool hemoccult results (5.4%) than did those who reported exposure (3.2%).

Prealbumin in its continuous form significantly decreased with age (p<0.001) and increased with current alcohol use (p<0.001). Covariate association tests for discretized prealbumin revealed significant associations with current alcohol use (p=0.003) and lifetime alcohol history (p=0.003). The prevalence of low prealbumin levels increased with current alcohol use. Heavy lifetime drinkers had a higher prevalence of low prealbumin levels (2.3%), followed by nondrinkers (1.7%) and moderate lifetime drinkers (0.6%).

Albumin in its continuous form was significantly associated with age (p<0.001) and degreasing chemical exposure (p=0.017). Albumin was inversely associated with age, and participants who reported exposure to degreasing chemicals had a lower mean albumin level than those who did not report exposure (4,185.8 mg/dl vs. 4,222.3 mg/dl). Dichotomized albumin was only significantly associated with current alcohol use (p=0.047). The percentage of participants with low albumin levels increased with current alcohol use.

Tests of covariate association for α-1-acid glycoprotein in its continuous form showed significant associations with occupation (p<0.001), current alcohol use (p<0.001), and lifetime alcohol history (p<0.001). Levels of α-1-acid glycoprotein increased with current alcohol use and lifetime alcohol history. Enlisted groundcrew had the highest mean α-1-acid glycoprotein level (86.34 mg/dl), followed by enlisted flyers (85.71 mg/dl) and officers (81.68 mg/dl).

The discrete form of α-1-acid glycoprotein was significantly associated with current alcohol use (p=0.003). The prevalence of high α-1-acid glycoprotein values increased as current alcohol use increased.

The continuous form of α-1-antitrypsin increased with age (p<0.001) and lifetime alcohol history (p=0.001) and decreased with current wine consumption (p<0.001). Race (p=0.006), occupation (p<0.001), industrial chemical exposure (p=0.001), and degreasing chemical exposure (p=0.023) also were significant. Non-Black participants had a higher mean α-1-antitrypsin level than did Black participants (148.3 mg/dl vs. 141.8 mg/dl). Enlisted flyers had the highest mean α-1-antitrypsin level

(153.0 mg/dl), followed by the enlisted groundcrew (150.2 mg/dl) and officers (143.4 mg/dl). In both industrial chemical exposure and degreasing chemical exposure, participants who reported exposure had higher mean α-1-antitrypsin levels.

The trichotomous form of α-1-antitrypsin was significantly associated with occupation ($p=0.022$), industrial chemical exposure ($p=0.037$), and current wine consumption ($p=0.031$). Officers had the highest percentage of abnormally low α-1-antitrypsin levels (2.3%), followed by enlisted groundcrew (0.9%) and enlisted flyers (0.6%). Enlisted flyers and enlisted groundcrew each had 0.9 percent abnormally high α-1-antitrypsin values, followed by officers with 0.2 percent abnormally high α-1-antitrypsin values. Participants who did not report exposure to industrial chemicals had a higher percentage of abnormally low α-1-antitrypsin levels (2.1%), as well as a higher percentage of abnormally high α-1-antitrypsin levels (0.9%) than participants who reported exposure to industrial chemicals (0.9 percent abnormally low and 0.5 percent abnormally high). Participants who currently drank wine had a higher percentage of abnormally low α-1-antitrypsin values than those who did not drink wine (1.9% vs. 1.0%). Participants who currently did not drink wine had a higher percentage of abnormally high α-1-antitrypsin values than did those who currently did drink wine (0.9% vs. 0.2%).

The continuous form of α-2-macroglobulin increased with age ($p<0.001$) and decreased with current alcohol use ($p=0.031$). Race and occupation were associated significantly with α-2-macroglobulin ($p<0.001$ and $p=0.013$, respectively). Non-Black participants had a higher mean α-2-macroglobulin level than did Black participants (172.2 mg/dl vs. 152.1 mg/dl). Enlisted flyers had the highest mean α-2-macroglobulin level (177.2 mg/dl), followed by officers (170.8 mg/dl) and enlisted groundcrew (169.0 mg/dl).

Tests of covariate association for discretized α-2-macroglobulin found significant covariate associations with age and lifetime alcohol history ($p=0.001$ each). The prevalence of high α-2-macroglobulin levels increased with age. Nondrinkers had the highest percentage of high α-1-macroglobulin levels, followed by heavy drinkers and moderate lifetime drinkers (9.3%, 3.3%, and 2.9%, respectively).

In its continuous form, tests of covariate association showed apolipoprotein B levels significantly decreased with age ($p=0.023$). Occupation also was associated significantly with apolipoprotein B ($p<0.001$). Enlisted flyers had the highest mean apolipoprotein B level (114.3 mg/dl), followed by the enlisted groundcrew (112.4 mg/dl) and officers (108.3 mg/dl). Apolipoprotein B in its discrete form showed a significant covariate association with occupation ($p=0.004$). Enlisted flyers had the highest prevalence of high apolipoprotein B values (56.1%), followed by enlisted groundcrew (53.7%) and officers (47.1%).

C3 complement in its continuous form decreased with age ($p=0.027$), current alcohol use ($p<0.001$), and lifetime alcohol history ($p=0.034$). Race ($p=0.002$), occupation ($p<0.001$), industrial chemical exposure ($p<0.001$), and degreasing chemical exposure ($p<0.001$) also were associated significantly with C3 complement. Non-Black participants had a lower mean C3 complement level than Black participants (118.4 mg/dl vs. 124.0 mg/dl). Officers had the lowest mean C3 complement level (114.7 mg/dl), followed by enlisted flyers (120.5 mg/dl) and enlisted groundcrew (121.6 mg/dl). For each of the industrial chemical exposure and degreasing chemical exposure covariates, participants who did not report exposure had lower mean C3 complement levels.

Current alcohol use was significantly associated with C3 complement in its discrete form ($p=0.001$). Participants who were currently moderate drinkers had the highest percentage of low C3 complement values (4.6%), followed by lighter drinkers (1.6%) and heavier drinkers (0.0%).

Tests of covariate association showed C4 complement in its continuous form to be significantly associated with race ($p<0.001$), occupation ($p<0.001$), and industrial chemical exposure ($p=0.029$). Non-Black participants had a lower mean C4 complement level than Black participants (25.65 mg/dl vs. 29.00 mg/dl). Officers had the lowest mean C4 complement level (25.21 mg/dl), followed by enlisted flyers (25.95 mg/dl) and enlisted groundcrew (26.35 mg/dl). Participants who did not report exposure to industrial chemicals had a lower mean C4 complement level than those who reported exposure (25.51 mg/dl vs. 26.02 mg/dl).

C4 complement in its discrete form was significantly associated with degreasing chemical exposure ($p=0.031$). Participants who did not report exposure had a higher prevalence of low C4 complement values (0.5%) than those who reported exposure (0.0%).

In its continuous form, tests of covariate association showed haptoglobin levels increased significantly with current alcohol use and lifetime alcohol history ($p=0.013$ and $p<0.001$, respectively). Occupation, industrial chemical exposure, and degreasing chemical exposure also were associated significantly with haptoglobin ($p<0.001$, $p=0.013$, and $p=0.001$, respectively). Enlisted flyers had the highest mean haptoglobin level (142.0 mg/dl), followed by enlisted groundcrew (136.3 mg/dl) and officers (118.7 mg/dl). In each of the industrial chemical exposure and degreasing chemical exposure covariates, participants who reported exposure had higher mean haptoglobin levels.

In its discrete form, tests of covariate association for haptoglobin showed similar results to the continuous analysis. Significant covariates were occupation ($p=0.001$), current alcohol use ($p=0.005$), lifetime alcohol history ($p=0.018$), industrial chemical exposure ($p=0.010$), and degreasing chemical exposure ($p=0.003$). Enlisted flyers had the highest percentage of high haptoglobin levels (36.1%), followed by enlisted groundcrew (33.8%) and officers (22.9%). The prevalence of high haptoglobin levels increased with current alcohol use. Heavy lifetime drinkers had the largest percentage of high haptoglobin values (34.2%), followed by nondrinkers (30.5%) and moderate lifetime drinkers (27.8%). In each of the analyses of industrial chemical exposure and degreasing chemical exposure, participants who reported exposure had a larger percentage of high haptoglobin levels.

Transferrin in its continuous form significantly decreased with age ($p=0.022$) and increased with current alcohol use ($p=0.022$). Also significantly associated with transferrin were race ($p<0.001$) and degreasing chemical exposure ($p=0.009$). Black participants had a lower mean transferrin level than non-Blacks (237.8 mg/dl vs. 251.7 mg/dl). Participants who reported exposure to degreasing chemicals had a lower mean transferrin level than those who were exposed (248.2 mg/dl vs. 252.4 mg/dl).

Tests of covariate association for discretized transferrin showed age and race to be significantly associated with transferrin ($p=0.043$ and $p=0.001$, respectively). Older participants had a higher prevalence of low transferrin levels than did younger participants (11.0% vs. 8.2%). Blacks had a higher percentage of low transferrin levels than non-Blacks (20.8% vs. 9.1%).

13.2.2 Exposure Analysis

The following section presents results of the statistical analyses of the dependent variables shown in Table 13-1. Dependent variables were derived from a medical records review and verification of self-reported gastrointestinal conditions, a 1997 physical examination determination of hepatomegaly, and numerous laboratory measurements conducted at the 1997 follow-up examination.

Four models were examined for each dependent variable given in Table 13-1. The analyses of these models are presented below. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7, respectively. These analyses were performed both unadjusted and adjusted for relevant covariates. Model 1 examined the relation between the dependent variable and group (i.e., Ranch Hand or Comparison). In this model, exposure was defined as "yes" for Ranch Hands and "no" for Comparisons

without regard to the magnitude of the exposure. As an attempt to quantify exposure, three contrasts of Ranch Hands and Comparisons were performed along with the overall Ranch Hand versus Comparison contrast. These three contrasts compared Ranch Hands and Comparisons within each occupational category (i.e., officers, enlisted flyers, and enlisted groundcrew). As described in previous reports, the average levels of exposure to dioxin were highest for enlisted groundcrew, followed by enlisted flyers, then officers.

Model 2 explored the relation between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 parts per trillion (ppt). If a participant did not have a 1987 dioxin level, the 1992 level was used to estimate the initial dioxin level. If a participant did not have a 1987 or a 1992 dioxin level, the 1997 level was used to estimate the initial dioxin level. A statistical adjustment for the percentage of body fat at the time of the participant's blood measurement of dioxin was included in this model to account for body-fat-related differences in elimination rate (66).

Model 3 divided the Ranch Hands examined in Model 2 into two categories based on their initial dioxin measures. These two categories are referred to as "low Ranch Hand" and "high Ranch Hand." Two additional categories, Ranch Hands with 1987 serum dioxin levels at or below 10 ppt and Comparisons with 1987 serum dioxin levels at or below 10 ppt, were formed and included in the model. Ranch Hands with 1987 serum dioxin levels at or below 10 ppt are referred to as the "background Ranch Hand" category. Dioxin levels in 1992 were used if the 1987 level was not available, and dioxin levels in 1997 were used if the 1987 and 1992 levels were not available. These four categories—Comparisons, background Ranch Hands, low Ranch Hands, and high Ranch Hands—were used in Model 3 analyses. The relation between the dependent variable in each of the three Ranch Hand categories and the dependent variable in the Comparison category was examined. A fourth contrast, exploring the relation of the dependent variable in the combined low and high Ranch Hand categories relative to Comparisons, also was conducted. This combination is referred to in the tables as the "low plus high Ranch Hand" category. As in Model 2, a statistical adjustment for the percentage of body fat at the time of the participant's blood measurement of dioxin was included in this model.

Model 4 examined the relation between the dependent variable and 1987 lipid-adjusted dioxin levels in all Ranch Hands with a dioxin measurement. If a participant did not have a 1987 dioxin measurement, the 1992 measurement was used to determine the dioxin level. If a participant did not have a 1987 or a 1992 dioxin measurement, the 1997 measurement was used to determine the dioxin level.

13.2.2.1 Medical Records Variables

13.2.2.1.1 Uncharacterized Hepatitis

All unadjusted and adjusted analyses of the appearance of uncharacterized hepatitis for Models 1 through 4 were nonsignificant (Table 13-3(a–h): $p>0.18$ for all analyses).

Table 13-3. Analysis of Uncharacterized Hepatitis

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***863***	***17 (2.0)***	***1.17 (0.61,2.23)***	***0.634***
	Comparison	***1,244***	***21 (1.7)***		
Officer	Ranch Hand	338	5 (1.5)	1.03 (0.32,3.28)	0.958
	Comparison	488	7 (1.4)		
Enlisted Flyer	Ranch Hand	151	4 (2.6)	1.67 (0.37,7.57)	0.507
	Comparison	187	3 (1.6)		
Enlisted Groundcrew	Ranch Hand	374	8 (2.1)	1.11 (0.44,2.78)	0.826
	Comparison	569	11 (1.9)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.18 (0.62,2.26)***	***0.617***
Officer	1.05 (0.33,3.35)	0.935
Enlisted Flyer	1.62 (0.35,7.40)	0.533
Enlisted Groundcrew	1.13 (0.45,2.85)	0.795

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	158	3 (1.9)	1.10 (0.67,1.80)	0.705
Medium	161	3 (1.9)		
High	159	3 (1.9)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
475	1.02 (0.58,1.79)	0.936

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race, industrial chemical exposure, and degreasing chemical exposure because of the sparse number of Ranch Hands with uncharacterized hepatitis.

Table 13-3. Analysis of Uncharacterized Hepatitis (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,206	21 (1.7)		
Background RH	378	8 (2.1)	1.27 (0.56,2.92)	0.568
Low RH	237	4 (1.7)	0.96 (0.33,2.82)	0.938
High RH	241	5 (2.1)	1.15 (0.43,3.10)	0.779
Low plus High RH	478	9 (1.9)	1.05 (0.48,2.32)	0.902

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,205		
Background RH	375	1.39 (0.59,3.27)	0.450
Low RH	236	1.00 (0.34,2.97)	0.999
High RH	239	1.04 (0.38,2.89)	0.932
Low plus High RH	475	1.02 (0.46,2.28)	0.957

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	287	6 (2.1)	0.86 (0.61,1.21)	0.377
Medium	283	5 (1.8)		
High	286	6 (2.1)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 13-3. Analysis of Uncharacterized Hepatitis (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
850	0.78 (0.55,1.12)	0.184

[a] Relative risk for a twofold increase in 1987 dioxin.

13.2.2.1.2 Jaundice (Unspecified)

The unadjusted Model 1 analysis revealed a significant overall group difference in the percentage of individuals with jaundice (Table 13-4(a): Est. RR=0.49, p=0.025). The percentage of Ranch Hands with jaundice was 1.4 percent versus 2.9 percent of the Comparisons. After stratifying by occupation, marginally significant differences were seen between Ranch Hand and Comparison officers, as well as enlisted groundcrew (Table 13-4(a): Est. RR=0.45, p=0.091; Est. RR=0.30, p=0.057, respectively). The percentage of officers and enlisted groundcrew with jaundice was higher among the Comparisons than the Ranch Hands.

Table 13-4. Analysis of Jaundice (Unspecified)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***846***	***12 (1.4)***	***0.49 (0.25,0.94)***	***0.025***
	Comparison	***1,219***	***35 (2.9)***		
Officer	Ranch Hand	329	6 (1.8)	0.45 (0.18,1.14)	0.091
	Comparison	478	19 (4.0)		
Enlisted Flyer	Ranch Hand	149	3 (2.0)	3.70 (0.38,35.9)	0.260
	Comparison	181	1 (0.6)		
Enlisted Groundcrew	Ranch Hand	368	3 (0.8)	0.30 (0.09,1.04)	0.057
	Comparison	560	15 (2.7)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.49 (0.25,0.96)***	***0.028***
Officer	0.46 (0.18,1.17)	0.103
Enlisted Flyer	3.47 (0.36,33.8)	0.284
Enlisted Groundcrew	0.29 (0.08,1.03)	0.055

Table 13-4. Analysis of Jaundice (Unspecified) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	154	0 (0.0)	1.03 (0.21,5.02)	0.973
Medium	160	1 (0.6)		
High	155	0 (0.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
466	1.01 (0.20,5.08)	0.995

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are adjusted only for percent body fat at the time of the blood measurement of dioxin and lifetime alcohol history because of the sparse number of Ranch Hands with jaundice.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,182	34 (2.9)		
Background RH	370	11 (3.0)	1.05 (0.52,2.11)	0.890
Low RH	232	0 (0.0)	--	0.017[c]
High RH	237	1 (0.4)	0.14 (0.02,1.04)	0.055
Low plus High RH	469	1 (0.2)	--	0.001[c]

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] P-value determined using a chi-square test with continuity correction because of the sparse number of Ranch Hands with unspecified jaundice.
--: Results not presented because of the sparse number of Ranch Hands with unspecified jaundice.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 13-4. Analysis of Jaundice (Unspecified) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,181		
Background RH	367	0.99 (0.49,2.03)	0.988
Low RH	231	--	--
High RH	235	0.16 (0.02,1.20)	0.075
Low plus High RH	466	--	--

[a] Relative risk and confidence interval relative to Comparisons.
--: Results not presented because of the sparse number of Ranch Hands with unspecified jaundice.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	281	8 (2.8)	0.44 (0.28,0.69)	<0.001
Medium	276	3 (1.1)		
High	282	1 (0.4)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
833	0.39 (0.24,0.65)	<0.001

[a] Relative risk for a twofold increase in 1987 dioxin.

After covariate adjustment, the overall group difference remained significant (Table 13-4(b): Adj. RR=0.49, p=0.028). Stratifying by occupation revealed a marginally significant difference between Ranch Hands and Comparisons among the enlisted groundcrew (Table 13-4(b): Adj. RR=0.29, p=0.055).

Only one Ranch Hand had an extrapolated initial dioxin value. The Model 2 unadjusted analysis of jaundice was not significant (Table 13-4(c): p=0.973), nor was the adjusted analysis (Table 13-4(d): p=0.995).

The Model 3 unadjusted and adjusted analyses of jaundice each revealed a marginally significant difference between Ranch Hands in the high dioxin category and Comparisons (Table 13-4(e,f): Est. RR=0.14, p=0.055, for the unadjusted analysis; Adj. RR=0.16, p=0.075, for the adjusted analysis). The percentage of Ranch Hands in the high dioxin category with jaundice was 0.4 percent versus 2.9

percent among the Comparisons. There were no Ranch Hands in the low dioxin category. Unadjusted chi-square tests of association revealed a significantly smaller percentage of Ranch Hands in the low dioxin category with jaundice than Comparisons (Table 13-4(e): p=0.017). A significantly smaller percentage of Ranch Hands in the low and high dioxin categories combined also had jaundice than did Comparisons (Table 13-4(e): p=0.001).

The unadjusted and adjusted Model 4 analyses revealed a significant relation between 1987 dioxin and jaundice (Table 13-4(g,h): Est. RR=0.44, p<0.001; Adj. RR=0.39, p<0.001, respectively). The percentages of participants with jaundice in the low, medium, and high 1987 dioxin categories were 2.8, 1.1, and 0.4, respectively.

13.2.2.1.3 Acute Necrosis of the Liver

Only one participant had an acute necrosis of the liver. The participant was a non-Black, Comparison officer. Further statistical analysis was not performed.

13.2.2.1.4 Chronic Liver Disease and Cirrhosis (Alcohol-related)

All unadjusted and adjusted analyses of alcohol-related chronic liver disease and cirrhosis were nonsignificant (Table 13-5(a–h): p>0.22 for all analyses).

Table 13-5. Analysis of Chronic Liver Disease and Cirrhosis (Alcohol-related)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***815***	***39 (4.8)***	***1.01 (0.67,1.54)***	***0.958***
	Comparison	***1,183***	***56 (4.7)***		
Officer	Ranch Hand	326	15 (4.6)	1.58 (0.75,3.32)	0.229
	Comparison	472	14 (3.0)		
Enlisted Flyer	Ranch Hand	138	7 (5.1)	0.75 (0.29,1.95)	0.553
	Comparison	180	12 (6.7)		
Enlisted Groundcrew	Ranch Hand	351	17 (4.8)	0.85 (0.46,1.57)	0.602
	Comparison	531	30 (5.6)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.93 (0.60,1.45)***	***0.762***
Officer	1.50 (0.71,3.19)	0.290
Enlisted Flyer	0.70 (0.26,1.88)	0.474
Enlisted Groundcrew	0.75 (0.39,1.45)	0.390

Table 13-5. Analysis of Chronic Liver Disease and Cirrhosis (Alcohol-related) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	152	7 (4.6)	1.06 (0.78,1.45)	0.708
Medium	151	8 (5.3)		
High	144	8 (5.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
444	1.06 (0.72,1.57)	0.765

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,147	54 (4.7)		
Background RH	361	16 (4.4)	0.97 (0.55,1.73)	0.924
Low RH	226	11 (4.9)	1.02 (0.53,1.99)	0.946
High RH	221	12 (5.4)	1.12 (0.59,2.14)	0.725
Low plus High RH	447	23 (5.1)	1.07 (0.65,1.77)	0.788

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 13-5. Analysis of Chronic Liver Disease and Cirrhosis (Alcohol-related) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Comparison	1,146		
Background RH	358	1.03 (0.56,1.90)	0.914
Low RH	225	0.95 (0.48,1.91)	0.894
High RH	219	0.88 (0.43,1.81)	0.734
Low plus High RH	444	0.92 (0.54,1.57)	0.755

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**	
1987 Dioxin	**n**	**Number (%) Yes**	**Estimated Relative Risk (95% C.I.)[a]**	**p-Value**
Low	273	12 (4.4)	1.10 (0.89,1.37)	0.368
Medium	269	15 (5.6)		
High	266	12 (4.5)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
802	1.09 (0.84,1.41)	0.506

[a] Relative risk for a twofold increase in 1987 dioxin.

13.2.2.1.5 Chronic Liver Disease and Cirrhosis (Non-alcohol-related)

All results from analysis of non-alcohol-related chronic liver disease and cirrhosis were nonsignificant (Table 13-6(a–h): p>0.21 for all analyses).

Table 13-6. Analysis of Chronic Liver Disease and Cirrhosis (Non-alcohol-related)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***870***	***14 (1.6)***	***1.44 (0.68,3.04)***	***0.336***
	Comparison	***1,250***	***14 (1.1)***		
Officer	Ranch Hand	341	5 (1.5)	2.43 (0.58,10.18)	0.226
	Comparison	493	3 (0.6)		
Enlisted Flyer	Ranch Hand	151	2 (1.3)	0.82 (0.14,4.99)	0.832
	Comparison	187	3 (1.6)		
Enlisted Groundcrew	Ranch Hand	378	7 (1.9)	1.33 (0.48,3.69)	0.589
	Comparison	570	8 (1.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.43 (0.68,3.03)***	***0.348***
Officer	2.47 (0.58,10.52)	0.219
Enlisted Flyer	0.77 (0.13,4.71)	0.777
Enlisted Groundcrew	1.32 (0.47,3.69)	0.598

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	2 (1.3)	1.02 (0.61,1.70)	0.949
Medium	162	4 (2.5)		
High	160	2 (1.3)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
479	1.04 (0.61,1.76)	0.897

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race because of the sparse number of Ranch Hands with a history of non-alcohol-related chronic liver disease and cirrhosis.

Table 13-6. Analysis of Chronic Liver Disease and Cirrhosis (Non-alcohol-related) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,212	14 (1.2)		
Background RH	381	6 (1.6)	1.64 (0.62,4.34)	0.321
Low RH	239	3 (1.3)	1.01 (0.29,3.58)	0.986
High RH	243	5 (2.1)	1.52 (0.53,4.32)	0.433
Low plus High RH	482	8 (1.7)	1.24 (0.50,3.06)	0.639

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,211		
Background RH	378	1.89 (0.68,5.25)	0.223
Low RH	238	1.15 (0.32,4.12)	0.829
High RH	241	1.37 (0.47,4.00)	0.568
Low plus High RH	479	1.26 (0.51,3.12)	0.625

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	4 (1.4)	1.05 (0.73,1.49)	0.803
Medium	287	4 (1.4)		
High	288	6 (2.1)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 13-6. Analysis of Chronic Liver Disease and Cirrhosis (Non-alcohol-related) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
857	1.02 (0.68,1.54)	0.920

[a] Relative risk for a twofold increase in 1987 dioxin.

13.2.2.1.6 Liver Abscess and Sequelae of Chronic Liver Disease

A sparse number of abnormalities restricted the analysis of liver abscess and sequelae of chronic liver disease. One non-Black, Ranch Hand enlisted groundcrew and one non-Black, Comparison officer were noted to have a liver abscess and sequelae of chronic liver disease. No significant relations with dioxin were noted in any of the Models 1 through 4 analyses (Table 13-7(a–h): p>0.16 for all analyses performed).

Table 13-7. Analysis of Liver Abscess and Sequelae of Chronic Liver Disease

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***870***	***1 (0.1)***	***1.44 (0.09,23.03)***	***0.798***
	Comparison	***1,251***	***1 (0.1)***		
Officer	Ranch Hand	341	0 (0.0)	--	0.999[a]
	Comparison	494	1 (0.2)		
Enlisted Flyer	Ranch Hand	151	0 (0.0)	--	--
	Comparison	187	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	378	1 (0.3)	--	0.836[a]
	Comparison	570	0 (0.0)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a history of a liver abscess and sequelae of chronic liver disease.
--: Results not presented because of the sparse number of participants with a liver abscess and sequelae of chronic liver disease.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.45 (0.09,23.24)***	***0.795***
Officer	--	--
Enlisted Flyer	--	--
Enlisted Groundcrew	--	--

--: Results not presented because of the sparse number of participants with a liver abscess and sequelae of chronic liver disease.

Note: Results are not adjusted for race and occupation because of the sparse number of participants with a liver abscess and sequelae of chronic liver disease.

Table 13-7. Analysis of Liver Abscess and Sequelae of Chronic Liver Disease (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	0 (0.0)	1.99 (0.64,6.25)	0.277
Medium	162	0 (0.0)		
High	160	1 (0.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)	p-Value
479	2.09 (0.61,7.19)	0.277

Note: Results are adjusted only for percent body fat at the time of the blood measurement of dioxin, age, and lifetime alcohol history because of the sparse number of Ranch Hands with a liver abscess and sequelae of chronic liver disease.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,213	1 (0.1)		
Background RH	381	0 (0.0)	--	0.999[c]
Low RH	239	0 (0.0)	--	0.999[c]
High RH	243	1 (0.4)	5.44 (0.33,89.44)	0.236
Low plus High RH	482	1 (0.2)	--	0.999[c]

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] P-value determined using a chi-square test with continuity correction because of the sparse number of Ranch Hands with a liver abscess and sequelae of chronic liver disease.
--: Results not presented because of the sparse number of Ranch Hands with a liver abscess and sequelae of chronic liver disease.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 13-7. Analysis of Liver Abscess and Sequelae of Chronic Liver Disease (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)**	**p-Value**
Comparison	1,212		
Background RH	378	--	--
Low RH	238	--	--
High RH	241	7.76 (0.38,158.28)	0.183
Low plus High RH	479	--	--

--: Analyses not performed because of the sparse number of Ranch Hands with a liver abscess and sequelae of chronic liver disease.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for race and occupation because of the sparse number of Ranch Hands with a liver abscess and sequelae of chronic liver disease.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**	
1987 Dioxin	**n**	**Number (%) Yes**	**Estimated Relative Risk (95% C.I.)[a]**	**p-Value**
Low	288	0 (0.0)	2.30 (0.71,7.43)	0.162
Medium	287	0 (0.0)		
High	288	1 (0.3)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	**Adjusted Relative Risk (95% C.I.)**	**p-Value**
857	2.05 (0.68,6.15)	0.212

Note: Results are adjusted only for age and lifetime alcohol history because of the sparse number of Ranch Hands with a liver abscess and sequelae of chronic liver disease.

13.2.2.1.7 Enlarged Liver (Hepatomegaly)

The unadjusted and adjusted Model 1 analyses of the prevalence of enlarged liver revealed no group differences when combining all occupations (Table 13-8(a,b): p>0.33 for each analysis). After stratifying by occupation, a marginally significant difference was seen between Ranch Hand and Comparison enlisted groundcrew (Table 13-8(a,b): Est. RR=0.30, p=0.056; Adj. RR=0.29, p=0.057, respectively). Among the enlisted groundcrew, 0.8 percent of the Ranch Hands had an enlarged liver versus 2.6 percent of the Comparisons. No significant results were seen in the Model 2, Model 3, or Model 4 analyses (Table 13-8(c–h): p>0.15 for all analyses).

Table 13-8. Analysis of Enlarged Liver (Hepatomegaly)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	**Group**	**n**	**Number (%) Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***869***	***14 (1.6)***	***0.74 (0.39,1.42)***	***0.361***
	Comparison	***1,249***	***27 (2.2)***		
Officer	Ranch Hand	341	5 (1.5)	0.80 (0.27,2.40)	0.689
	Comparison	492	9 (1.8)		
Enlisted Flyer	Ranch Hand	151	6 (4.0)	2.54 (0.62,10.32)	0.193
	Comparison	187	3 (1.6)		
Enlisted Groundcrew	Ranch Hand	377	3 (0.8)	0.30 (0.09,1.03)	0.056
	Comparison	570	15 (2.6)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	**Adjusted Relative Risk (95% C.I.)**	**p-Value**
All	***0.73 (0.38,1.41)***	***0.339***
Officer	0.78 (0.26,2.36)	0.662
Enlisted Flyer	2.53 (0.62,10.38)	0.198
Enlisted Groundcrew	0.29 (0.08,1.03)	0.057

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Number (%) Yes**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	160	2 (1.3)	0.96 (0.56,1.65)	0.880
Medium	162	4 (2.5)		
High	159	2 (1.3)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
478	0.91 (0.46,1.80)	0.790

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race because of the sparse number of Ranch Hands with a history of an enlarged liver.

Table 13-8. Analysis of Enlarged Liver (Hepatomegaly) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	26 (2.1)		
Background RH	381	6 (1.6)	0.75 (0.31,1.86)	0.540
Low RH	239	2 (0.8)	0.38 (0.09,1.62)	0.191
High RH	242	6 (2.5)	1.12 (0.46,2.78)	0.798
Low plus High RH	481	8 (1.7)	0.66 (0.27,1.61)	0.357

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,210		
Background RH	378	0.80 (0.32,2.01)	0.630
Low RH	238	0.35 (0.08,1.51)	0.159
High RH	240	1.09 (0.42,2.79)	0.864
Low plus High RH	478	0.62 (0.25,1.54)	0.302

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	4 (1.4)	0.94 (0.65,1.35)	0.731
Medium	287	4 (1.4)		
High	287	6 (2.1)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 13-8. Analysis of Enlarged Liver (Hepatomegaly) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
856	0.93 (0.60,1.46)	0.753

[a] Relative risk for a twofold increase in 1987 dioxin.

13.2.2.1.8 Other Liver Disorders

Both the unadjusted and adjusted Model 1 analyses revealed marginally significant differences between Ranch Hands and Comparisons over all occupations (Table 13-9(a,b): Est. RR=1.20, p=0.067; Adj. RR=1.19, p=0.090, respectively). The percentage of Ranch Hands with other liver disorders was 28.8 versus 25.2 for Comparisons. Stratifying by occupation revealed a marginally significant difference between Ranch Hands and Comparisons within the enlisted groundcrew stratum for both the unadjusted and adjusted analyses (Table 13-9(a,b): Est. RR=1.32, p=0.062; Adj. RR=1.31, p=0.073, respectively). Of the enlisted groundcrew Ranch Hands, 30.8 percent had other liver disorders versus 25.2 percent of the Comparisons.

Table 13-9. Analysis of Other Liver Disorders

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***249 (28.8)***	***1.20 (0.99,1.46)***	***0.067***
	Comparison	***1,240***	***312 (25.2)***		
Officer	Ranch Hand	338	93 (27.5)	1.15 (0.84,1.57)	0.399
	Comparison	486	121 (24.9)		
Enlisted Flyer	Ranch Hand	151	40 (26.5)	1.04 (0.64,1.70)	0.864
	Comparison	187	48 (25.7)		
Enlisted Groundcrew	Ranch Hand	377	116 (30.8)	1.32 (0.99,1.76)	0.062
	Comparison	567	143 (25.2)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.19 (0.97,1.45)***	***0.090***
Officer	1.15 (0.83,1.57)	0.400
Enlisted Flyer	0.98 (0.60,1.61)	0.933
Enlisted Groundcrew	1.31 (0.98,1.75)	0.073

Table 13-9. Analysis of Other Liver Disorders (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	159	39 (24.5)	1.12 (0.97,1.30)	0.119
Medium	162	53 (32.7)		
High	160	55 (34.4)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
478	1.23 (1.03,1.47)	0.022

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,202	299 (24.9)		
Background RH	378	99 (26.2)	1.15 (0.88,1.50)	0.318
Low RH	238	64 (26.9)	1.09 (0.80,1.50)	0.578
High RH	243	83 (34.2)	1.49 (1.10,2.00)	0.009
Low plus High RH	481	147 (30.6)	1.28 (1.01,1.62)	0.042

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,201		
Background RH	375	1.13 (0.86,1.49)	0.371
Low RH	237	1.05 (0.76,1.45)	0.757
High RH	241	1.52 (1.11,2.08)	0.009
Low plus High RH	478	1.27 (1.00,1.62)	0.055

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 13-9. Analysis of Other Liver Disorders (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	286	73 (25.5)	1.10 (1.00,1.22)	0.055
Medium	285	76 (26.7)		
High	288	97 (33.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤ 7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
853	1.11 (0.99,1.25)	0.077

[a] Relative risk for a twofold increase in 1987 dioxin.

The unadjusted Model 2 analysis did not reveal a significant association between initial dioxin and other liver disorders (Table 13-9(c): p=0.119). After adjusting for covariates, the results became significant (Table 13-9(d): Adj. RR=1.23, p=0.022). The percentages of other liver disorders in the low, medium, and high initial dioxin categories were 24.5, 32.7, and 34.4, respectively.

The unadjusted Model 3 analysis of other liver disorders revealed significant differences between Ranch Hands in the high dioxin category and Comparisons, as well as between Ranch Hands in the low and high dioxin categories combined and Comparisons (Table 13-9(e): Est. RR=1.49, p=0.009; Est. RR=1.28, p=0.042, respectively). The same contrasts were significant after adjusting for covariates (Table 13-9(f): Adj. RR=1.52, p=0.009, for Ranch Hands in the high dioxin category versus Comparisons; Adj. RR=1.27, p=0.055, for Ranch Hands in the low and high dioxin categories combined versus Comparisons). The percentages of other liver disorders among Ranch Hands in the high dioxin category, Ranch Hands in the low and high dioxin categories combined, and Comparisons were 34.2, 30.6, and 24.9, respectively.

Both the unadjusted and adjusted Model 4 analyses revealed marginally significant positive associations between 1987 dioxin and other liver disorders (Table 13-9(g,h): Est. RR=1.10, p=0.055; Adj. RR=1.11, p=0.077, respectively). The percentages of other liver disorders in the low, medium, and high 1987 dioxin categories were 25.5, 26.7, and 33.7, respectively.

13.2.2.2 Physical Examination Variables

13.2.2.2.1 Current Hepatomegaly

All unadjusted and adjusted analyses of current hepatomegaly, as assessed by a physician at the 1997 physical examination, were nonsignificant for Models 1 through 4 (Table 13-10: p>0.10 for each analysis).

Table 13-10. Analysis of Current Hepatomegaly

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***860***	***10 (1.2)***	***2.06 (0.78,5.43)***	***0.141***
	Comparison	***1,231***	***7 (0.6)***		
Officer	Ranch Hand	340	4 (1.2)	2.90 (0.53,15.95)	0.220
	Comparison	490	2 (0.4)		
Enlisted Flyer	Ranch Hand	150	2 (1.3)	--	0.389[a]
	Comparison	185	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	370	4 (1.1)	1.20 (0.32,4.51)	0.783
	Comparison	556	5 (0.9)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with current hepatomegaly.
--: Results not presented because of the sparse number of participants with current hepatomegaly.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)[a]	p-Value
All	***2.13 (0.80,5.67)***	***0.127***
Officer	3.17 (0.57,17.56)	0.187
Enlisted Flyer	--	--
Enlisted Groundcrew	1.18 (0.31,4.51)	0.805

--: Results not presented because of the sparse number of participants with current hepatomegaly.

Note: Results are not adjusted for race because of the sparse number of participants with current hepatomegaly.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	158	3 (1.9)	0.69 (0.36,1.31)	0.223
Medium	159	3 (1.9)		
High	160	1 (0.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
474	0.66 (0.30,1.45)	0.279

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race because of the sparse number of participants with current hepatomegaly.

Table 13-10. Analysis of Current Hepatomegaly (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,194	7 (0.6)		
Background RH	376	3 (0.8)	1.53 (0.39,5.99)	0.543
Low RH	236	3 (1.3)	2.10 (0.54,8.23)	0.284
High RH	241	4 (1.7)	2.58 (0.74,8.97)	0.136
Low plus High RH	477	7 (1.5)	2.33 (0.80,6.76)	0.119

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,193		
Background RH	374	1.64 (0.40,6.69)	0.489
Low RH	235	2.26 (0.57,9.01)	0.247
High RH	239	2.62 (0.70,9.84)	0.154
Low plus High RH	474	2.44 (0.82,7.24)	0.109

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for race because of the sparse number of participants with current hepatomegaly.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	283	3 (1.1)	1.04 (0.69,1.58)	0.853
Medium	285	3 (1.1)		
High	285	4 (1.4)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 13-10. Analysis of Current Hepatomegaly (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
848	1.05 (0.64,1.74)	0.838

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race because of the sparse number of participants with current hepatomegaly.

13.2.2.3 Laboratory Examination Variables

13.2.2.3.1 AST (Continuous)

Model 1 showed no significant difference in mean AST levels between Ranch Hands and Comparisons in either the unadjusted or adjusted analysis (Table 13-11(a,b): p>0.44 for all contrasts). The unadjusted and adjusted analyses for Model 2 did not reveal any significant relations between initial dioxin and AST levels (Table 13-11(c,d): p>0.49 in both analyses).

Table 13-11. Analysis of AST (U/l) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***859***	***23.01***	***0.13 --***	***0.705***
	Comparison	***1,231***	***22.88***		
Officer	Ranch Hand	340	23.40	0.06 --	0.914
	Comparison	490	23.34		
Enlisted Flyer	Ranch Hand	150	22.17	–0.32 --	0.696
	Comparison	185	22.48		
Enlisted Groundcrew	Ranch Hand	369	22.99	0.39 --	0.447
	Comparison	556	22.60		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 13-11. Analysis of AST (U/l) (Continuous) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***854***	***23.36***	***0.18 --***	***0.597***
	Comparison	***1,229***	***23.17***		
Officer	Ranch Hand	340	23.88	0.08 --	0.885
	Comparison	489	23.80		
Enlisted Flyer	Ranch Hand	148	22.79	–0.09 --	0.916
	Comparison	184	22.87		
Enlisted Groundcrew	Ranch Hand	366	23.32	0.37 --	0.470
	Comparison	556	22.95		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	158	23.39	23.50	0.011	0.003 (0.012)	0.813
Medium	159	23.71	23.72			
High	159	23.43	23.32			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of AST versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	158	24.76	0.057	0.010 (0.014)	0.493
Medium	158	25.53			
High	157	24.99			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of AST versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 13-11. Analysis of AST (U/l) (Continuous) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	**n**	**Mean[a]**	**Adj. Mean[ab]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]**	**p-Value[d]**
Comparison	1,194	22.85	22.84		
Background RH	376	22.34	22.54	–0.30 --	0.501
Low RH	236	23.45	23.39	0.55 --	0.306
High RH	240	23.56	23.36	0.52 --	0.334
Low plus High RH	476	23.51	23.37	0.53 --	0.193

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	**n**	**Adj. Mean[a]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]**	**p-Value[c]**
Comparison	1,193	23.23		
Background RH	374	22.76	–0.47 --	0.305
Low RH	235	23.93	0.70 --	0.207
High RH	238	24.17	0.94 --	0.100
Low plus High RH	473	24.05	0.82 --	0.055

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin +1)**		
1987 Dioxin	**n**	**Mean[a]**	**R^2**	**Adjusted Slope (Std. Error)[b]**	**p-Value**
Low	283	22.29	0.005	0.017 (0.008)	0.033
Medium	285	23.30			
High	284	23.38			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of AST versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 13-11. Analysis of AST (U/l) (Continuous) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**		
1987 Dioxin	**n**	**Adj. Mean[a]**	**R^2**	**Adjusted Slope (Std. Error)[b]**	**p-Value**
Low	283	22.72	0.036	0.028 (0.009)	0.002
Medium	283	24.06			
High	281	24.66			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of AST versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

The Model 3 unadjusted analysis of AST showed no significant difference between any of the Ranch Hand categories and the Comparison group (Table 13-11(e): p>0.19 for all contrasts). After covariate adjustment, a marginally significant difference between the mean AST of Ranch Hands in the high dioxin category and the Comparison mean was revealed (Table 13-11(f): difference of adjusted means=0.94 U/l, p=0.100). The adjusted mean levels of AST for Ranch Hands in the high dioxin category and the Comparison group were 24.17 U/l and 23.23 U/l, respectively. A marginally significant difference between Ranch Hands in the low and high dioxin categories combined and the Comparisons also was seen after covariate adjustment (Table 13-11(f): difference of adjusted means=0.82 U/l, p=0.055). The adjusted mean levels of AST for Ranch Hands in the low and high dioxin categories combined and the Comparison group were 24.05 U/l and 23.23 U/l, respectively.

In Model 4, the unadjusted analysis found a significant positive association between AST in its continuous form and 1987 dioxin levels (Table 13-11(g): slope=0.017, p=0.033). The adjusted Model 4 analysis revealed a significant association between AST levels and 1987 dioxin levels (Table 13-11(h): adjusted slope=0.028, p=0.002). The adjusted mean AST levels in the low, medium, and high 1987 dioxin categories were 22.72 U/l, 24.06 U/l, and 24.66 U/l, respectively.

13.2.2.3.2 AST (Discrete)

The unadjusted and adjusted Model 1 analyses did not show a significant group difference in the percentage of individuals with high AST levels (Table 13-12(a,b): p>0.25 for all contrasts).

Table 13-12. Analysis of AST (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	**Group**	**n**	**Number (%) High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***859***	***63 (7.3)***	***1.11 (0.79,1.56)***	***0.552***
	Comparison	***1,231***	***82 (6.7)***		
Officer	Ranch Hand	340	24 (7.1)	1.09 (0.63,1.88)	0.765
	Comparison	490	32 (6.5)		
Enlisted Flyer	Ranch Hand	150	10 (6.7)	0.75 (0.33,1.72)	0.501
	Comparison	185	16 (8.6)		
Enlisted Groundcrew	Ranch Hand	369	29 (7.9)	1.31 (0.78,2.19)	0.304
	Comparison	556	34 (6.1)		

Table 13-12. Analysis of AST (Discrete) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.14 (0.81,1.61)***	***0.448***
Officer	1.09 (0.63,1.89)	0.763
Enlisted Flyer	0.84 (0.36,1.92)	0.671
Enlisted Groundcrew	1.35 (0.81,2.28)	0.252

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	158	11 (7.0)	1.08 (0.86,1.36)	0.498
Medium	159	20 (12.6)		
High	159	14 (8.8)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
473	1.13 (0.86,1.50)	0.380

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,194	79 (6.6)		
Background RH	376	17 (4.5)	0.72 (0.42,1.24)	0.241
Low RH	236	19 (8.1)	1.21 (0.72,2.04)	0.476
High RH	240	26 (10.8)	1.60 (1.00,2.56)	0.051
Low plus High RH	476	45 (9.5)	1.39 (0.95,2.05)	0.094

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 13-12. Analysis of AST (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,193		
Background RH	374	0.70 (0.40,1.22)	0.212
Low RH	235	1.28 (0.75,2.18)	0.360
High RH	238	1.79 (1.08,2.96)	0.024
Low plus High RH	473	1.51 (1.02,2.26)	0.041

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	283	11 (3.9)	1.26 (1.06,1.48)	0.008
Medium	285	23 (8.1)		
High	284	28 (9.9)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
847	1.38 (1.12,1.71)	0.002

[a] Relative risk for a twofold increase in 1987 dioxin.

In Model 2, neither the unadjusted nor adjusted analyses showed significant associations between AST and initial dioxin (Table 13-12(c,d): p≥0.38 for both analyses).

The unadjusted Model 3 analysis of AST in its discrete form revealed two marginally significant contrasts: Ranch Hands in the high dioxin category versus Comparisons and Ranch Hands in the low and high dioxin categories combined versus Comparisons (Table 13-12(e): Est. RR=1.60, p=0.051; Est. RR=1.39, p=0.094, respectively). Similarly, the adjusted analysis showed a significant difference between Ranch Hands in the high dioxin category and Comparisons (Table 13-12(f): Adj. RR=1.79, p=0.024), as well as between the Ranch Hands in the low and high dioxin categories combined and Comparisons (Adj. RR=1.51, p=0.041). The percentages of individuals with high levels of AST among the Ranch Hands in the high dioxin category, Ranch Hands in the low and high dioxin categories combined, and Comparisons were 10.8, 9.5, and 6.6, respectively.

The unadjusted analysis for Model 4 showed a significant association between AST in its discrete form and 1987 dioxin (Table 13-12(g): Est. RR=1.26, p=0.008). Similarly, the adjusted analysis revealed significant results (Adj. RR=1.38, p=0.002). The percentages of participants with high AST levels in the low, medium, and high 1987 dioxin categories were 3.9, 8.1, and 9.9, respectively.

13.2.2.3.3 ALT (Continuous)

All Model 1 and 2 analyses of ALT in its continuous form showed nonsignificant results (Table 13-13(a–d): p>0.19 for each analysis).

Table 13-13. Analysis of ALT (U/l) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	**Group**	**n**	**Mean[a]**	**Difference of Means (95% C.I.)[b]**	**p-Value[c]**
All	***Ranch Hand***	***859***	***42.58***	***0.13 --***	***0.803***
	Comparison	***1,231***	***42.45***		
Officer	Ranch Hand	340	42.21	0.42 --	0.613
	Comparison	490	41.79		
Enlisted Flyer	Ranch Hand	150	41.21	−1.38 --	0.290
	Comparison	185	42.59		
Enlisted Groundcrew	Ranch Hand	369	43.50	0.51 --	0.537
	Comparison	556	42.99		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	**Group**	**n**	**Adj. Mean[a]**	**Difference of Adj. Means (95% C.I.)[b]**	**p-Value[c]**
All	***Ranch Hand***	***854***	***42.29***	***0.20 --***	***0.707***
	Comparison	***1,229***	***42.09***		
Officer	Ranch Hand	340	42.75	0.61 --	0.460
	Comparison	489	42.14		
Enlisted Flyer	Ranch Hand	148	41.72	−1.12 --	0.386
	Comparison	184	42.84		
Enlisted Groundcrew	Ranch Hand	366	41.96	0.30 --	0.698
	Comparison	556	41.66		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 13-13. Analysis of ALT (U/l) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	158	42.39	42.65	0.036	0.013 (0.010)	0.199
Medium	159	44.97	45.00			
High	159	45.02	44.72			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of ALT versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	158	44.34	0.094	0.011 (0.012)	0.357
Medium	158	47.03			
High	157	46.08			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of ALT versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,194	42.41	42.37		
Background RH	376	40.74	41.32	−1.05 --	0.129
Low RH	236	43.32	43.14	0.77 --	0.368
High RH	240	44.91	44.27	1.90 --	0.027
Low plus High RH	476	44.12	43.71	1.34 --	0.041

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 13-13. Analysis of ALT (U/l) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,193	42.21		
Background RH	374	41.31	–0.90 --	0.192
Low RH	235	43.65	1.44 --	0.084
High RH	238	43.62	1.41 --	0.098
Low plus High RH	473	43.63	1.42 --	0.026

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	41.17	0.023	0.029 (0.007)	<0.001
Medium	285	41.87			
High	284	44.82			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of ALT versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	40.98	0.079	0.033 (0.007)	<0.001
Medium	283	42.50			
High	281	45.28			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of ALT versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

The unadjusted Model 3 analysis of ALT revealed two significant contrasts: Ranch Hands in the high dioxin category versus Comparisons and Ranch Hands in the low and high dioxin categories combined versus Comparisons (Table 13-13(e): difference of means=1.90 U/l, p=0.027; difference of means=1.34 U/l, p=0.041, respectively).

After covariate adjustment, the Model 3 analysis of ALT revealed marginally significant differences between the adjusted mean of Ranch Hands in the low dioxin category and the Comparison adjusted mean (Table 13-13(f): difference of adjusted means=1.44 U/l, p=0.084) and between the adjusted mean of Ranch Hands in the high dioxin category and the Comparison adjusted mean (difference of adjusted means=1.41 U/l, p=0.098). Ranch Hands in the low and high dioxin categories combined also were significantly different from the Comparisons in the adjusted analysis (difference of adjusted means=1.42 U/l, p=0.026). Ranch Hands in the low and high dioxin categories combined had higher mean ALT levels (43.65 U/l and 43.62 U/l) than did the Comparisons (42.21 U/l).

The unadjusted and adjusted analyses for Model 4 each showed significant positive associations between ALT in its continuous form and 1987 dioxin (Table 13-13(g,h): slope=0.029, p<0.001, unadjusted; slope=0.033, p<0.001, adjusted). The adjusted mean ALT levels in the low, medium, and high 1987 dioxin categories were 40.98 U/l, 42.50 U/l, and 45.28 U/l, respectively.

13.2.2.3.4 ALT (Discrete)

The Model 1 analyses of ALT in its discrete form revealed no significant differences between Ranch Hands and Comparisons when examined across all occupations and within each occupation (Table 13-14(a,b): p>0.13 for each contrast).

Table 13-14. Analysis of ALT (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	**Group**	**n**	**Number (%) High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***859***	***68 (7.9)***	***1.13 (0.81,1.57)***	***0.468***
	Comparison	***1,231***	***87 (7.1)***		
Officer	Ranch Hand	340	23 (6.8)	1.54 (0.85,2.82)	0.157
	Comparison	490	22 (4.5)		
Enlisted Flyer	Ranch Hand	150	15 (10.0)	0.97 (0.48,1.98)	0.935
	Comparison	185	19 (10.3)		
Enlisted Groundcrew	Ranch Hand	369	30 (8.1)	0.98 (0.61,1.59)	0.938
	Comparison	556	46 (8.3)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	**Adjusted Relative Risk (95% C.I.)**	**p-Value**
All	***1.12 (0.80,1.57)***	***0.495***
Officer	1.58 (0.86,2.89)	0.138
Enlisted Flyer	0.97 (0.46,2.01)	0.927
Enlisted Groundcrew	0.97 (0.60,1.57)	0.889

Table 13-14. Analysis of ALT (Discrete) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	158	10 (6.3)	1.17 (0.95,1.45)	0.140
Medium	159	21 (13.2)		
High	159	19 (11.9)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
473	1.32 (1.00,1.73)	0.049

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,194	85 (7.1)		
Background RH	376	17 (4.5)	0.67 (0.39,1.15)	0.145
Low RH	236	20 (8.5)	1.18 (0.71,1.97)	0.522
High RH	240	30 (12.5)	1.74 (1.11,2.71)	0.015
Low plus High RH	476	50 (10.5)	1.43 (0.99,2.08)	0.058

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,193		
Background RH	374	0.71 (0.41,1.23)	0.223
Low RH	235	1.30 (0.77,2.18)	0.323
High RH	238	1.53 (0.95,2.45)	0.080
Low plus High RH	473	1.41 (0.96,2.07)	0.079

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 13-14. Analysis of ALT (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	283	15 (5.3)	1.33 (1.13,1.56)	0.001
Medium	285	18 (6.3)		
High	284	34 (12.0)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
847	1.48 (1.20,1.83)	<0.001

[a] Relative risk for a twofold increase in 1987 dioxin.

The association between initial dioxin and ALT examined in the unadjusted Model 2 analysis revealed nonsignificant results (Table 13-14(c): p=0.140). After covariate adjustment, a significant association was revealed (Table 13-14(d): Adj. RR=1.32, p=0.049). The percentages of high ALT levels in the low, medium, and high initial dioxin categories were 6.3, 13.2, and 11.9, respectively.

The unadjusted Model 3 analysis of ALT in its discrete form revealed two significant contrasts: Ranch Hands in the high dioxin category versus Comparisons and Ranch Hands in the low and high dioxin categories combined versus Comparisons (Table 13-14(e): Est. RR=1.74, p=0.015; Est. RR=1.43, p=0.058, respectively). The percentages of individuals with high ALT levels among Ranch Hands in the high dioxin category, Ranch Hands in the low and high dioxin categories combined, and Comparisons were 12.5, 10.5, and 7.1, respectively. The same two contrasts were marginally significant after adjusting for covariates (Table 13-14(f): Adj. RR=1.53, p=0.080; Adj. RR=1.41, p=0.079).

The Model 4 unadjusted and adjusted analyses each revealed a significant association between 1987 dioxin and ALT in its discrete form (Table 13-14(g,h): Est. RR=1.33, p=0.001; Adj. RR=1.48, p<0.001). The percentages of participants with high ALT values in the low, medium, and high 1987 dioxin categories were 5.3, 6.3, and 12.0, respectively.

13.2.2.3.5 GGT (Continuous)

All analysis results from Models 1 and 2 of GGT were nonsignificant (Table 13-15(a–d): p>0.22 for each analysis). The unadjusted Model 3 analysis of GGT revealed significant differences between Ranch Hands in the high dioxin category and Comparisons, as well as between Ranch Hands in the low and high dioxin categories combined and Comparisons (Table 13-15(e): difference of means=5.17 U/l, p=0.003; difference of means=3.46 U/l, p=0.007, respectively). The same contrasts were significant after adjusting for covariates (Table 13-15(f): difference of adjusted means=5.00 U/l, p=0.006, for Ranch Hands in the high dioxin category versus Comparisons; difference of adjusted means=3.71 U/l, p=0.006, for Ranch Hands in the low and high dioxin categories combined versus Comparisons). The adjusted mean GGT levels for Ranch Hands in the high dioxin category, Ranch Hands in the low and high dioxin categories combined, and Comparisons were 50.40 U/l, 49.11 U/l, and 45.40 U/l, respectively.

A significant association was revealed between GGT and 1987 dioxin in the Model 4 unadjusted analysis (Table 13-15(g): slope=0.040, p=0.002). Similarly, the adjusted analysis found a significant association between GGT levels and 1987 dioxin (Table 13-15(h): adjusted slope=0.042, p=0.003). The adjusted mean GGT levels were 42.89 U/l for the low dioxin category, 45.65 U/l for the medium dioxin category, and 50.85 U/l for the high dioxin category.

Table 13-15. Analysis of GGT (U/l) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***859***	***43.62***	***1.01 --***	***0.340***
	Comparison	***1,231***	***42.61***		
Officer	Ranch Hand	340	42.32	1.57 --	0.332
	Comparison	490	40.74		
Enlisted Flyer	Ranch Hand	150	44.45	–0.84 --	0.758
	Comparison	185	45.29		
Enlisted Groundcrew	Ranch Hand	369	44.52	1.09 --	0.506
	Comparison	556	43.44		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***854***	***46.80***	***1.33 --***	***0.223***
	Comparison	***1,229***	***45.47***		
Officer	Ranch Hand	340	45.24	1.62 --	0.331
	Comparison	489	43.62		
Enlisted Flyer	Ranch Hand	148	48.28	0.62 --	0.826
	Comparison	184	47.66		
Enlisted Groundcrew	Ranch Hand	366	46.67	1.28 --	0.439
	Comparison	556	45.39		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 13-15. Analysis of GGT (U/l) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	158	43.87	44.19	0.013	0.004 (0.019)	0.823
Medium	159	48.89	48.92			
High	159	46.22	45.86			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of GGT versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	158	48.46	0.097	0.008 (0.022)	0.709
Medium	158	52.52			
High	157	50.18			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of GGT versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,194	42.26	42.21		
Background RH	376	39.99	40.81	−1.40 --	0.296
Low RH	236	44.27	43.99	1.78 --	0.283
High RH	240	48.36	47.38	5.17 --	0.003
Low plus High RH	476	46.29	45.67	3.46 --	0.007

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 13-15. Analysis of GGT (U/l) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,193	45.40		
Background RH	374	44.67	-0.73 --	0.606
Low RH	235	47.84	2.43 --	0.159
High RH	238	50.40	5.00 --	0.006
Low plus High RH	473	49.11	3.71 --	0.006

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	40.35	0.012	0.040 (0.013)	0.002
Medium	285	42.53			
High	284	47.59			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of GGT versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	42.89	0.103	0.042 (0.014)	0.003
Medium	283	45.65			
High	281	50.85			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of GGT versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

13.2.2.3.6 GGT (Discrete)

The unadjusted and adjusted analysis results for Models 1 and 2 showed no significant results (Table 13-16(a–d): p≥0.31 for each analysis).

A marginally significant difference between Ranch Hands in the low and high dioxin categories combined and Comparisons was revealed in both the unadjusted and adjusted Model 3 analyses (Table 13-16(e,f): Est. RR=1.33, p=0.094, for the unadjusted analysis; Adj. RR=1.38, p=0.065, for the adjusted analysis). The percentage of abnormal GGT values among Ranch Hands in the low and high dioxin categories combined was 13.0 versus 9.8 among the Comparisons.

Table 13-16. Analysis of GGT (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***89 (10.4)***	***1.03 (0.77,1.38)***	***0.831***
	Comparison	***1,231***	***124 (10.1)***		
Officer	Ranch Hand	340	31 (9.1)	1.23 (0.75,2.02)	0.419
	Comparison	490	37 (7.6)		
Enlisted Flyer	Ranch Hand	150	23 (15.3)	1.16 (0.63,2.14)	0.637
	Comparison	185	25 (13.5)		
Enlisted Groundcrew	Ranch Hand	369	35 (9.5)	0.83 (0.54,1.29)	0.419
	Comparison	556	62 (11.2)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.08 (0.80,1.45)***	***0.604***
Officer	1.24 (0.75,2.06)	0.399
Enlisted Flyer	1.39 (0.73,2.65)	0.310
Enlisted Groundcrew	0.86 (0.55,1.35)	0.512

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	158	17 (10.8)	1.00 (0.81,1.22)	0.964
Medium	159	28 (17.6)		
High	159	17 (10.7)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 13-16. Analysis of GGT (Discrete) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
473	1.06 (0.82,1.37)	0.669

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,194	117 (9.8)		
Background RH	376	25 (6.6)	0.70 (0.45,1.10)	0.122
Low RH	236	29 (12.3)	1.27 (0.82,1.96)	0.283
High RH	240	33 (13.8)	1.38 (0.91,2.10)	0.127
Low plus High RH	476	62 (13.0)	1.33 (0.95,1.84)	0.094

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,193		
Background RH	374	0.77 (0.48,1.23)	0.273
Low RH	235	1.42 (0.91,2.22)	0.127
High RH	238	1.35 (0.86,2.11)	0.186
Low plus High RH	473	1.38 (0.98,1.95)	0.065

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	283	21 (7.4)	1.17 (1.01,1.35)	0.034
Medium	285	27 (9.5)		
High	284	39 (13.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 13-16. Analysis of GGT (Discrete) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
847	1.27 (1.05,1.53)	0.012

[a] Relative risk for a twofold increase in 1987 dioxin.

In Model 4, both unadjusted and adjusted analyses showed significant positive associations with 1987 dioxin (Table 13-16(g,h): Est. RR=1.17, p=0.034; Adj. RR=1.27, p=0.012, respectively). The percentages of high GGT levels in the low, medium, and high 1987 dioxin categories were 7.4, 9.5, and 13.7, respectively.

13.2.2.3.7 Alkaline Phosphatase (Continuous)

Both the unadjusted and adjusted Model 1 analyses of alkaline phosphatase revealed significant overall group differences (Table 13-17(a,b): difference of means=2.16 U/l, p=0.024; difference of adjusted means=2.32 U/l, p=0.016). The overall adjusted mean alkaline phosphatase values were 82.77 U/l and 80.46 U/l for Ranch Hands and Comparisons, respectively. After stratifying by occupation, unadjusted and adjusted analyses revealed group differences within the enlisted groundcrew stratum (unadjusted: difference of means=3.18 U/l, p=0.030; adjusted: difference of adjusted means=3.43 U/l, p=0.021). Within the enlisted groundcrew stratum, the Ranch Hands had an adjusted mean alkaline phosphatase of 85.11 U/l versus 81.68 U/l for the Comparisons.

Table 13-17. Analysis of Alkaline Phosphatase (U/l) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***859***	***81.81***	***2.16 --***	***0.024***
	Comparison	***1,231***	***79.65***		
Officer	Ranch Hand	340	78.44	1.70 --	0.241
	Comparison	490	76.74		
Enlisted Flyer	Ranch Hand	150	83.79	0.34 --	0.889
	Comparison	185	83.45		
Enlisted Groundcrew	Ranch Hand	369	84.22	3.18 --	0.030
	Comparison	556	81.04		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 13-17. Analysis of Alkaline Phosphatase (U/l) (Continuous) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***856***	***82.77***	***2.32 --***	***0.016***
	Comparison	***1,229***	***80.46***		
Officer	Ranch Hand	340	78.68	1.80 --	0.215
	Comparison	489	76.88		
Enlisted Flyer	Ranch Hand	149	84.06	0.58 --	0.811
	Comparison	184	83.47		
Enlisted Groundcrew	Ranch Hand	367	85.11	3.43 --	0.021
	Comparison	556	81.68		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	158	81.73	81.97	0.009	–0.004 (0.009)	0.646
Medium	159	83.60	83.63			
High	159	80.51	80.25			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of alkaline phosphatase versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	158	80.72	0.037	–0.021 (0.011)	0.053
Medium	158	79.95			
High	158	75.04			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of alkaline phosphatase versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 13-17. Analysis of Alkaline Phosphatase (U/l) (Continuous) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,194	79.58	79.57		
Background RH	376	81.35	81.50	1.93 --	0.130
Low RH	236	82.39	82.34	2.78 --	0.070
High RH	240	81.50	81.36	1.79 --	0.238
Low plus High RH	476	81.94	81.85	2.28 --	0.051

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,193	80.38		
Background RH	375	83.86	3.48 --	0.008
Low RH	235	83.18	2.79 --	0.071
High RH	239	80.32	–0.06 --	0.967
Low plus High RH	474	81.72	1.34 --	0.255

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	81.36	<0.001	–0.004 (0.006)	0.555
Medium	285	81.39			
High	284	82.29			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of alkaline phosphatase versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 13-17. Analysis of Alkaline Phosphatase (U/l) (Continuous) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	80.95	0.042	–0.021 (0.007)	0.003
Medium	284	80.09			
High	282	77.40			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of alkaline phosphatase versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

The Model 2 unadjusted analysis of alkaline phosphatase was nonsignificant (Table 13-17(c): p=0.646). The adjusted analysis revealed a marginally significant inverse association between alkaline phosphatase and initial dioxin (Table 13-17(d): adjusted slope=–0.021, p=0.053). Mean alkaline phosphatase levels in the low, medium, and high initial dioxin categories were 80.72 U/l, 79.95 U/l, and 75.04 U/l, respectively.

The unadjusted Model 3 analysis of alkaline phosphatase revealed two marginally significant contrasts: Ranch Hands in the low dioxin category versus Comparisons (Table 13-17(e): difference of means=2.78 U/l, p=0.070) and Ranch Hands in the low and high dioxin categories combined versus Comparisons (difference of means=2.28 U/l, p=0.051). The adjusted analysis showed significant differences between Ranch Hands in the background dioxin category and Comparisons (Table 13-17(f): difference of adjusted means=3.48 U/l, p=0.008), as well as a marginally significant difference between Ranch Hands in the low dioxin category and Comparisons (difference of adjusted means=2.79 U/l, p=0.071). Ranch Hands in the background and low dioxin categories had higher mean alkaline phosphatase levels than the Comparisons (83.86 U/l for the Ranch Hands in the background dioxin category and 83.18 U/l for the Ranch Hands in the low dioxin category versus 80.38 U/l for Comparisons).

The unadjusted analysis of Model 4 showed no significant association between alkaline phosphatase and 1987 dioxin levels (Table 13-17(g): p=0.555). After covariate adjustment, a significant inverse relation was revealed (Table 13-17(h): adjusted slope=–0.021, p=0.003). The adjusted mean alkaline phosphatase values in the low, medium, and high 1987 dioxin categories were 80.95 U/l, 80.09 U/l, and 77.40 U/l, respectively.

13.2.2.3.8 Alkaline Phosphatase (Discrete)

The unadjusted and adjusted Model 1 analyses of alkaline phosphatase in its discrete form showed no overall group difference between Ranch Hands and Comparisons (Table 13-18(a,b): p>0.33 for each analysis). Stratifying by occupation revealed a marginally significant group difference within the enlisted groundcrew stratum for both the unadjusted and adjusted analyses (Table 13-18(a,b): Est. RR=2.30, p=0.071; Adj. RR=2.46, p=0.053). The percentage of enlisted groundcrew with high alkaline phosphatase levels among the Ranch Hands was 3.3 percent versus 1.4 percent among the Comparisons. All analyses for Models 2 and 3 were nonsignificant (Table 13-18(c–f): p>0.10 for each analysis).

Table 13-18. Analysis of Alkaline Phosphatase (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***22 (2.6)***	***1.32 (0.74,2.37)***	***0.352***
	Comparison	***1,231***	***24 (1.9)***		
Officer	Ranch Hand	340	4 (1.2)	0.47 (0.15,1.48)	0.200
	Comparison	490	12 (2.4)		
Enlisted Flyer	Ranch Hand	150	6 (4.0)	1.89 (0.52,6.81)	0.333
	Comparison	185	4 (2.2)		
Enlisted Groundcrew	Ranch Hand	369	12 (3.3)	2.30 (0.93,5.69)	0.071
	Comparison	556	8 (1.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.34 (0.74,2.42)***	***0.332***
Officer	0.45 (0.14,1.41)	0.172
Enlisted Flyer	2.03 (0.56,7.40)	0.284
Enlisted Groundcrew	2.46 (0.99,6.13)	0.053

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	158	3 (1.9)	0.99 (0.60,1.65)	0.971
Medium	159	4 (2.5)		
High	159	2 (1.3)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
474	1.04 (0.61,1.76)	0.897

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results not adjusted for occupation because of the sparse number of participants with a high alkaline phosphatase level.

Table 13-18. Analysis of Alkaline Phosphatase (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,194	21 (1.8)		
Background RH	376	12 (3.2)	1.76 (0.85,3.63)	0.127
Low RH	236	4 (1.7)	0.97 (0.33,2.86)	0.960
High RH	240	5 (2.1)	1.24 (0.46,3.33)	0.670
Low plus High RH	476	9 (1.9)	1.10 (0.50,2.43)	0.815

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,193		
Background RH	375	1.85 (0.88,3.90)	0.104
Low RH	235	0.91 (0.31,2.71)	0.871
High RH	239	1.23 (0.44,3.41)	0.688
Low plus High RH	474	1.06 (0.48,2.37)	0.883

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	283	9 (3.2)	0.79 (0.58,1.09)	0.144
Medium	285	6 (2.1)		
High	284	6 (2.1)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
849	0.69 (0.50,0.94)	0.020

[a] Relative risk for a twofold increase in 1987 dioxin.

The Model 4 unadjusted analysis did not show significant results (Table 13-18(g): p=0.144). The adjusted analysis revealed a significant inverse relation between alkaline phosphatase and 1987 dioxin levels (Table 13-18(h): Adj. RR=0.69, p=0.020). The percentages of abnormal alkaline phosphatase values in the low, medium, and high 1987 dioxin categories were 3.2, 2.1, and 2.1, respectively.

13.2.2.3.9 Total Bilirubin (Continuous)

All unadjusted and adjusted Model 1 through Model 4 analyses of total bilirubin in its continuous form were nonsignificant (Table 13-19(a–h): p>0.36 for each analysis).

Table 13-19. Analysis of Total Bilirubin (mg/dl) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***859***	***0.518***	***–0.002 --***	***0.857***
	Comparison	***1,231***	***0.520***		
Officer	Ranch Hand	340	0.546	0.003 --	0.887
	Comparison	490	0.543		
Enlisted Flyer	Ranch Hand	150	0.489	–0.023 --	0.365
	Comparison	185	0.513		
Enlisted Groundcrew	Ranch Hand	369	0.506	0.003 --	0.869
	Comparison	556	0.503		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***854***	***0.511***	***–0.000 --***	***0.963***
	Comparison	***1,229***	***0.511***		
Officer	Ranch Hand	340	0.528	0.000 --	0.993
	Comparison	489	0.528		
Enlisted Flyer	Ranch Hand	148	0.487	–0.018 --	0.482
	Comparison	184	0.505		
Enlisted Groundcrew	Ranch Hand	366	0.512	0.006 --	0.727
	Comparison	556	0.507		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 13-19. Analysis of Total Bilirubin (mg/dl) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	158	0.524	0.527	0.013	–0.014 (0.016)	0.368
Medium	159	0.503	0.503			
High	159	0.514	0.510			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of total bilirubin versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	158	0.522	0.038	0.004 (0.019)	0.822
Medium	158	0.511			
High	157	0.532			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of total bilirubin versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,194	0.520	0.520		
Background RH	376	0.523	0.526	0.006 --	0.673
Low RH	236	0.517	0.516	–0.004 --	0.828
High RH	240	0.510	0.506	–0.014 --	0.418
Low plus High RH	476	0.513	0.511	–0.009 --	0.500

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 13-19. Analysis of Total Bilirubin (mg/dl) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,193	0.517		
Background RH	374	0.515	–0.002 --	0.901
Low RH	235	0.514	–0.003 --	0.884
High RH	238	0.520	0.003 --	0.861
Low plus High RH	473	0.517	0.000 --	0.981

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	0.526	0.001	–0.007 (0.011)	0.499
Medium	285	0.518			
High	284	0.509			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of total bilirubin versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	0.521	0.023	0.008 (0.012)	0.519
Medium	283	0.516			
High	281	0.532			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of total bilirubin versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

13.2.2.3.10 Total Bilirubin (Discrete)

All analysis results of total bilirubin in its dichotomous form were nonsignificant (Table 13-20(a–h): p>0.11 for each analysis).

Table 13-20. Analysis of Total Bilirubin (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***46 (5.4)***	***0.86 (0.59,1.25)***	***0.430***
	Comparison	***1,231***	***76 (6.2)***		
Officer	Ranch Hand	340	22 (6.5)	0.90 (0.52,1.56)	0.707
	Comparison	490	35 (7.1)		
Enlisted Flyer	Ranch Hand	150	8 (5.3)	1.10 (0.41,2.93)	0.846
	Comparison	185	9 (4.9)		
Enlisted Groundcrew	Ranch Hand	369	16 (4.3)	0.74 (0.40,1.37)	0.342
	Comparison	556	32 (5.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.86 (0.58,1.25)***	***0.420***
Officer	0.90 (0.52,1.57)	0.723
Enlisted Flyer	1.15 (0.43,3.08)	0.779
Enlisted Groundcrew	0.71 (0.38,1.33)	0.286

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	158	12 (7.6)	0.77 (0.54,1.09)	0.118
Medium	159	5 (3.1)		
High	159	7 (4.4)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
473	0.75 (0.49,1.13)	0.154

[a] Relative risk for a twofold increase in initial dioxin.

Table 13-20. Analysis of Total Bilirubin (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,194	74 (6.2)		
Background RH	376	21 (5.6)	0.91 (0.55,1.51)	0.724
Low RH	236	15 (6.4)	1.02 (0.58,1.81)	0.940
High RH	240	9 (3.8)	0.58 (0.29,1.18)	0.131
Low plus High RH	476	24 (5.0)	0.77 (0.47,1.25)	0.286

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,193		
Background RH	374	0.88 (0.53,1.47)	0.619
Low RH	235	1.03 (0.58,1.84)	0.919
High RH	238	0.59 (0.27,1.27)	0.175
Low plus High RH	473	0.78 (0.47,1.29)	0.331

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	283	18 (6.4)	0.89 (0.72,1.10)	0.275
Medium	285	15 (5.3)		
High	284	12 (4.2)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
847	0.94 (0.73,1.21)	0.646

[a] Relative risk for a twofold increase in 1987 dioxin.

13.2.2.3.11 Direct Bilirubin

In each of the unadjusted and adjusted analyses of Models 1 through 4, no significant associations were seen between dioxin and direct bilirubin (Table 13-21(a–h): p>0.19 for each contrast). Because of a sparse number of participants with a high direct bilirubin level, the analysis was limited in some of the models.

Table 13-21. Analysis of Direct Bilirubin

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***1 (0.1)***	***0.29 (0.03,2.45)***	***0.196***
	Comparison	***1,231***	***5 (0.4)***		
Officer	Ranch Hand	340	1 (0.3)	0.48 (0.05,4.62)	0.524
	Comparison	490	3 (0.6)		
Enlisted Flyer	Ranch Hand	150	0 (0.0)	--	--
	Comparison	185	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	369	0 (0.0)	--	0.667[a]
	Comparison	556	2 (0.4)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a high direct bilirubin level.

--: Results not presented because of the sparse number of participants with a high direct bilirubin level.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.32 (0.04,2.82)***	***0.254***
Officer	0.50 (0.05,4.90)	0.551
Enlisted Flyer	--	--
Enlisted Groundcrew	--	--

--: Results not presented because of the sparse number of participants with a high direct bilirubin level.

Note: Results for analysis across all occupational categories are not adjusted for occupation because of the sparse number of participants with a high direct bilirubin level.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	158	0 (0.0)	--	--
Medium	159	0 (0.0)		
High	159	0 (0.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

--: Results not presented because of the sparse number of Ranch Hands with a high direct bilirubin level.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 13-21. Analysis of Direct Bilirubin (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)	p-Value
--	--	--

--: Results not presented because of the sparse number of Ranch Hands with a high direct bilirubin level.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,194	5 (0.4)		
Background RH	376	1 (0.3)	0.88 (0.10,7.75)	0.906
Low RH	236	0 (0.0)	--	0.695[c]
High RH	240	0 (0.0)	--	0.686[c]
Low plus High RH	476	0 (0.0)	--	0.359[c]

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] P-value determined using a chi-square test with continuity correction because of the sparse number of Ranch Hands with a high direct bilirubin level.

--: Results not presented because of the sparse number of Ranch Hands with a high direct bilirubin level.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,193		
Background RH	374	1.09 (0.12,10.31)	0.937
Low RH	235	--	--
High RH	238	--	--
Low plus High RH	473	--	--

[a] Relative risk and confidence interval relative to Comparisons.

--: Results not presented because of the sparse number of Ranch Hands with a high direct bilirubin level.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for occupation because of the sparse number of Ranch Hands with a high direct bilirubin level.

Table 13-21. Analysis of Direct Bilirubin (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	283	0 (0.0)	0.78 (0.18,3.33)	0.735
Medium	285	1 (0.4)		
High	284	0 (0.0)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
847	0.79 (0.17,3.72)	0.764

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are adjusted only for age and lifetime alcohol history because of the sparse number of Ranch Hands with a high direct bilirubin level.

13.2.2.3.12 Lactic Dehydrogenase (Continuous)

The unadjusted and adjusted analyses of Models 1 through 4 showed no significant associations between dioxin and lactic dehydrogenase in its continuous form (Table 13-22(a–h): p>0.18 for each analysis).

Table 13-22. Analysis of Lactic Dehydrogenase (U/l) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***859***	***154.0***	***0.3 --***	***0.822***
	Comparison	***1,229***	***153.8***		
Officer	Ranch Hand	340	153.9	–0.5 --	0.799
	Comparison	489	154.4		
Enlisted Flyer	Ranch Hand	150	152.3	–0.3 --	0.927
	Comparison	184	152.5		
Enlisted Groundcrew	Ranch Hand	369	154.9	1.2 --	0.488
	Comparison	556	153.7		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 13-22. Analysis of Lactic Dehydrogenase (U/l) (Continuous) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***854***	***155.3***	***0.3 --***	***0.790***
	Comparison	***1,227***	***155.0***		
Officer	Ranch Hand	340	154.8	–0.6 --	0.768
	Comparison	488	155.3		
Enlisted Flyer	Ranch Hand	148	153.1	–0.8 --	0.787
	Comparison	183	153.9		
Enlisted Groundcrew	Ranch Hand	366	157.8	1.5 --	0.397
	Comparison	556	156.3		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	158	155.7	156.0	0.009	–0.001 (0.006)	0.908
Medium	159	152.4	152.4			
High	159	156.0	155.6			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of lactic dehydrogenase versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	158	159.1	0.036	0.000 (0.007)	0.979
Medium	158	156.8			
High	157	160.1			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of lactic dehydrogenase versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 13-22. Analysis of Lactic Dehydrogenase (U/l) (Continuous) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,192	153.8	153.7		
Background RH	376	153.1	154.3	0.6 --	0.693
Low RH	236	153.9	153.6	–0.1 --	0.941
High RH	240	155.4	154.1	0.4 --	0.816
Low plus High RH	476	154.7	153.8	0.1 --	0.916

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,192	155.5		
Background RH	374	156.1	0.6 --	0.737
Low RH	235	155.0	–0.5 --	0.774
High RH	238	156.8	1.3 --	0.528
Low plus High RH	473	155.9	0.4 --	0.812

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	152.7	0.002	0.005 (0.004)	0.211
Medium	285	155.3			
High	284	153.9			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of lactic dehydrogenase versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 13-22. Analysis of Lactic Dehydrogenase (U/l) (Continuous) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	154.3	0.015	0.006 (0.005)	0.187
Medium	283	156.4			
High	281	155.4			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of lactic dehydrogenase versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

13.2.2.3.13 Lactic Dehydrogenase (Discrete)

Lactic dehydrogenase in its dichotomized form showed nonsignificant results in all of the Models 1 through 4 unadjusted and adjusted analyses (Table 13-23(a–h): p>0.21 for each analysis).

Table 13-23. Analysis of Lactic Dehydrogenase (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***81 (9.4)***	***0.89 (0.66,1.19)***	***0.424***
	Comparison	***1,229***	***129 (10.5)***		
Officer	Ranch Hand	340	32 (9.4)	0.85 (0.54,1.36)	0.506
	Comparison	489	53 (10.8)		
Enlisted Flyer	Ranch Hand	150	13 (8.7)	1.07 (0.49,2.32)	0.866
	Comparison	184	15 (8.2)		
Enlisted Groundcrew	Ranch Hand	369	36 (9.8)	0.88 (0.57,1.35)	0.555
	Comparison	556	61 (11.0)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.90 (0.67,1.21)***	***0.479***
Officer	0.86 (0.54,1.37)	0.530
Enlisted Flyer	1.03 (0.47,2.24)	0.945
Enlisted Groundcrew	0.90 (0.58,1.39)	0.625

Table 13-23. Analysis of Lactic Dehydrogenase (Discrete) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	158	17 (10.8)	0.96 (0.75,1.21)	0.709
Medium	159	10 (6.3)		
High	159	16 (10.1)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
473	0.98 (0.74,1.30)	0.889

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,192	123 (10.3)		
Background RH	376	36 (9.6)	1.05 (0.71,1.57)	0.794
Low RH	236	21 (8.9)	0.81 (0.50,1.33)	0.406
High RH	240	22 (9.2)	0.77 (0.47,1.25)	0.291
Low plus High RH	476	43 (9.0)	0.79 (0.55,1.15)	0.214

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,191		
Background RH	374	1.07 (0.72,1.61)	0.729
Low RH	235	0.80 (0.48,1.31)	0.366
High RH	238	0.81 (0.49,1.34)	0.416
Low plus High RH	473	0.80 (0.55,1.17)	0.255

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 13-23. Analysis of Lactic Dehydrogenase (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	283	27 (9.5)	1.00 (0.85,1.17)	0.989
Medium	285	30 (10.5)		
High	284	22 (7.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
847	1.01 (0.84,1.21)	0.892

[a] Relative risk for a twofold increase in 1987 dioxin.

13.2.2.3.14 Cholesterol (Continuous)

The Model 1 unadjusted and adjusted analyses showed no significant association between group and cholesterol (Table 13-24(a,b): p>0.14 for each analysis).

Table 13-24. Analysis of Cholesterol (mg/dl) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***859***	***211.4***	***–0.3 --***	***0.838***
	Comparison	***1,231***	***211.7***		
Officer	Ranch Hand	340	206.2	–3.8 --	0.149
	Comparison	490	210.0		
Enlisted Flyer	Ranch Hand	150	215.0	–1.3 --	0.760
	Comparison	185	216.3		
Enlisted Groundcrew	Ranch Hand	369	214.7	3.0 --	0.239
	Comparison	556	211.8		

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

Table 13-24. Analysis of Cholesterol (mg/dl) (Continuous) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***854***	***212.3***	***–0.3 --***	***0.850***
	Comparison	***1,229***	***212.6***		
Officer	Ranch Hand	340	206.6	–3.8 --	0.141
	Comparison	489	210.4		
Enlisted Flyer	Ranch Hand	148	215.3	–1.2 --	0.781
	Comparison	184	216.4		
Enlisted Groundcrew	Ranch Hand	366	214.6	3.2 --	0.197
	Comparison	556	211.4		

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	158	205.9	205.7	0.017	0.129 (0.046)	0.005
Medium	159	215.1	215.1			
High	159	217.9	218.2			

[a] Transformed from square root scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on square root of cholesterol versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	158	209.0	0.044	0.083 (0.054)	0.122
Medium	158	215.9			
High	157	217.4			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of cholesterol versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 13-24. Analysis of Cholesterol (mg/dl) (Continuous) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,194	211.7	211.7		
Background RH	376	209.4	208.8	–2.9 --	0.183
Low RH	236	209.1	209.3	–2.4 --	0.351
High RH	240	216.8	217.4	5.7 --	0.032
Low plus High RH	476	213.0	213.4	1.7 --	0.422

[a] Transformed from square root scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[d] P-value is based on difference of means on square root scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,193	212.9		
Background RH	374	211.0	–1.9 --	0.392
Low RH	235	210.6	–2.3 --	0.389
High RH	238	217.3	4.4 --	0.115
Low plus High RH	473	214.0	1.1 --	0.616

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	210.9	0.008	0.077 (0.030)	0.009
Medium	285	206.6			
High	284	216.6			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of cholesterol versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 13-24. Analysis of Cholesterol (mg/dl) (Continuous) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	214.9	0.023	0.046 (0.034)	0.178
Medium	283	209.6			
High	281	216.8			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of cholesterol versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

The unadjusted Model 2 analysis revealed a significant positive association between initial dioxin and cholesterol (Table 13-24(c): slope=0.129, p=0.005). After covariate adjustment, the relation became nonsignificant (Table 13-24(d): p=0.122).

A significant difference between Ranch Hands in the high dioxin category and Comparisons was found in the unadjusted Model 3 analysis of cholesterol (Table 13-24(e): difference of means=5.7 mg/dl, p=0.032). The adjusted analysis revealed no significant contrasts (Table 13-24(f): p>0.11 for each contrast).

Model 4 unadjusted analysis results showed a significant association between 1987 dioxin and cholesterol in its continuous form (Table 13-24(g): slope=0.077, p=0.009). The adjusted analysis results were nonsignificant (Table 13-24(h): p=0.178).

13.2.2.3.15 Cholesterol (Discrete)

No significant difference between Ranch Hands and Comparisons was revealed in either the unadjusted or adjusted Model 1 analysis of cholesterol (Table 13-25(a,b): p>0.16 for each contrast).

Table 13-25. Analysis of Cholesterol (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***130 (15.1)***	***1.03 (0.81,1.31)***	***0.826***
	Comparison	***1,231***	***182 (14.8)***		
Officer	Ranch Hand	340	39 (11.5)	0.80 (0.53,1.22)	0.310
	Comparison	490	68 (13.9)		
Enlisted Flyer	Ranch Hand	150	22 (14.7)	0.96 (0.53,1.77)	0.905
	Comparison	185	28 (15.1)		
Enlisted Groundcrew	Ranch Hand	369	69 (18.7)	1.26 (0.89,1.78)	0.198
	Comparison	556	86 (15.5)		

Table 13-25. Analysis of Cholesterol (Discrete) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.04 (0.82,1.34)***	***0.726***
Officer	0.80 (0.53,1.23)	0.312
Enlisted Flyer	1.00 (0.54,1.83)	0.993
Enlisted Groundcrew	1.28 (0.90,1.82)	0.167

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	158	19 (12.0)	1.21 (1.01,1.45)	0.036
Medium	159	31 (19.5)		
High	159	32 (20.1)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
473	1.23 (0.99,1.52)	0.062

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,194	177 (14.8)		
Background RH	376	48 (12.8)	0.80 (0.56,1.12)	0.195
Low RH	236	34 (14.4)	0.98 (0.66,1.46)	0.915
High RH	240	48 (20.0)	1.51 (1.06,2.16)	0.023
Low plus High RH	476	82 (17.2)	1.22 (0.91,1.63)	0.183

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 13-25. Analysis of Cholesterol (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,193		
Background RH	374	0.85 (0.60,1.21)	0.379
Low RH	235	1.01 (0.68,1.51)	0.964
High RH	238	1.41 (0.97,2.04)	0.071
Low plus High RH	473	1.19 (0.89,1.60)	0.240

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	283	40 (14.1)	1.15 (1.02,1.30)	0.025
Medium	285	32 (11.2)		
High	284	58 (20.4)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
847	1.08 (0.93,1.24)	0.312

[a] Relative risk for a twofold increase in 1987 dioxin.

The unadjusted Model 2 analysis found a significant association between cholesterol and initial dioxin (Table 13-25(c): Est. RR=1.21, p=0.036). Similarly, the adjusted Model 2 analysis was marginally significant (Table 13-25(d): Adj. RR=1.23, p=0.062). The percentages of participants with high cholesterol levels in the low, medium, and high initial dioxin categories were 12.0, 19.5, and 20.1, respectively.

The Model 3 unadjusted analysis of cholesterol revealed a significant difference between Ranch Hands in the high dioxin category and Comparisons (Table 13-25(e): Est. RR=1.51, p=0.023) and a marginally significant difference in the adjusted analysis (Table 13-25(f): Adj. RR=1.41, p=0.071). The percentage of Ranch Hands in the high dioxin category was 20.0 versus 14.8 in the Comparison category.

The Model 4 unadjusted analysis showed a significant relation between 1987 dioxin and cholesterol level (Table 13-25(g): Est. RR=1.15, p=0.025). After adjusting for covariates, the results became nonsignificant (Table 13-25(h): p=0.312).

13.2.2.3.16 HDL Cholesterol (Continuous)

The unadjusted Model 1 analysis of HDL cholesterol showed no group difference between Ranch Hands and Comparisons (Table 13-26(a): p≥0.24 for each analysis). Although the adjusted analysis showed no overall group difference, stratifying by occupation revealed a marginally significant difference between Ranch Hands and Comparisons among the enlisted flyer stratum (Table 13-26(b): difference of means=2.29 mg/dl, p=0.078). The adjusted mean HDL cholesterol level for enlisted flyers in the Ranch Hand group was 47.56 mg/dl versus 45.28 mg/dl for the enlisted flyers in the Comparison group. Models 2 and 3 unadjusted and adjusted analyses showed no significant relations between dioxin and HDL cholesterol (Table 13-26(c–f): p≥0.13 for each analysis).

The unadjusted Model 4 analysis revealed a significant association between 1987 dioxin and HDL cholesterol (Table 13-26(g): slope=–0.023, p<0.001). Similarly, the adjusted Model 4 analysis results were significant (Table 13-26(h): adjusted slope=–0.014, p=0.037). Both analyses showed a decrease in HDL cholesterol levels as 1987 dioxin increased. The adjusted mean HDL cholesterol levels were 49.22 mg/dl, 46.80 mg/dl, and 46.31 mg/dl in the low, medium, and high 1987 dioxin categories, respectively.

Table 13-26. Analysis of HDL Cholesterol (mg/dl) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***858***	***44.97***	***0.13 --***	***0.805***
	Comparison	***1,230***	***44.84***		
Officer	Ranch Hand	340	46.64	–0.04 --	0.965
	Comparison	489	46.68		
Enlisted Flyer	Ranch Hand	149	45.07	1.49 --	0.240
	Comparison	185	43.58		
Enlisted Groundcrew	Ranch Hand	369	43.44	–0.25 --	0.739
	Comparison	556	43.69		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***853***	***47.08***	***0.28 --***	***0.600***
	Comparison	***1,228***	***46.81***		
Officer	Ranch Hand	340	48.76	–0.10 --	0.907
	Comparison	488	48.86		
Enlisted Flyer	Ranch Hand	147	47.56	2.29 --	0.078
	Comparison	184	45.28		
Enlisted Groundcrew	Ranch Hand	366	45.68	–0.13 --	0.866
	Comparison	556	45.81		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 13-26. Analysis of HDL Cholesterol (mg/dl) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	157	45.03	44.73	0.053	–0.009 (0.009)	0.312
Medium	159	43.33	43.30			
High	159	43.32	43.64			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of HDL cholesterol versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	157	46.09	0.132	0.005 (0.010)	0.625
Medium	158	44.96			
High	157	46.38			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of HDL cholesterol versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,193	44.75	44.79		
Background RH	376	46.34	45.54	0.75 --	0.269
Low RH	235	44.98	45.23	0.44 --	0.585
High RH	240	42.83	43.58	–1.21 --	0.130
Low plus High RH	475	43.88	44.39	–0.40 --	0.519

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 13-26. Analysis of HDL Cholesterol (mg/dl) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,192	46.77		
Background RH	374	47.11	0.34 --	0.628
Low RH	234	47.10	0.33 --	0.687
High RH	238	46.77	0.00 --	0.999
Low plus High RH	472	46.93	0.16 --	0.795

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for $\log_2$ (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	47.12	0.016	–0.023 (0.006)	<0.001
Medium	284	44.60			
High	284	43.23			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of HDL cholesterol versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for $\log_2$ (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	49.22	0.081	–0.014 (0.007)	0.037
Medium	282	46.80			
High	281	46.31			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of HDL cholesterol versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

13.2.2.3.17 HDL Cholesterol (Discrete)

All Model 1 analyses of HDL cholesterol in its discrete form were nonsignificant (Table 13-27(a,b): p>0.42 for each analysis).

The association between initial dioxin and HDL cholesterol examined in the unadjusted Model 2 analysis revealed nonsignificant results (Table 13-27(c): p=0.249). After adjusting for covariates, a significant association was shown (Table 13-27(d): Adj. RR=0.72, p=0.029). The percentages of low HDL cholesterol levels in the low, medium, and high initial dioxin categories were 8.3, 10.1, and 5.7, respectively.

Table 13-27. Analysis of HDL Cholesterol (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	**Group**	**n**	**Number (%) Low**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***858***	***71 (8.3)***	***1.14 (0.83,1.58)***	***0.421***
	Comparison	***1,230***	***90 (7.3)***		
Officer	Ranch Hand	340	19 (5.6)	1.15 (0.62,2.13)	0.664
	Comparison	489	24 (4.9)		
Enlisted Flyer	Ranch Hand	149	16 (10.7)	1.12 (0.55,2.27)	0.762
	Comparison	185	18 (9.7)		
Enlisted Groundcrew	Ranch Hand	369	36 (9.8)	1.14 (0.73,1.80)	0.561
	Comparison	556	48 (8.7)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	**Adjusted Relative Risk (95% C.I.)**	**p-Value**
All	***1.13 (0.81,1.57)***	***0.473***
Officer	1.15 (0.62,2.15)	0.650
Enlisted Flyer	0.98 (0.47,2.04)	0.957
Enlisted Groundcrew	1.18 (0.74,1.87)	0.483

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Number (%) Low**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	157	13 (8.3)	0.86 (0.66,1.12)	0.249
Medium	159	16 (10.1)		
High	159	9 (5.7)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
472	0.72 (0.53,0.98)	0.029

[a] Relative risk for a twofold increase in initial dioxin.

Table 13-27. Analysis of HDL Cholesterol (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Low	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,193	88 (7.4)		
Background RH	376	33 (8.8)	1.35 (0.88,2.05)	0.170
Low RH	235	19 (8.1)	1.07 (0.64,1.80)	0.798
High RH	240	19 (7.9)	0.98 (0.58,1.65)	0.937
Low plus High RH	475	38 (8.0)	1.02 (0.69,1.53)	0.910

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,192		
Background RH	374	1.57 (1.00,2.45)	0.049
Low RH	234	1.09 (0.64,1.84)	0.761
High RH	238	0.80 (0.47,1.37)	0.416
Low plus High RH	472	0.93 (0.62,1.40)	0.731

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Low	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	283	23 (8.1)	0.92 (0.78,1.09)	0.349
Medium	284	27 (9.5)		
High	284	21 (7.4)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
846	0.82 (0.68,0.98)	0.029

[a] Relative risk for a twofold increase in 1987 dioxin.

The unadjusted Model 3 analysis of HDL cholesterol did not show any of the Ranch Hand categories to be significantly different from the Comparison group (Table 13-27(e): $p \geq 0.17$ for all contrasts). In the adjusted analysis, a significant difference between Comparisons and Ranch Hands in the background dioxin category was revealed (Table 13-27(f): Adj. RR=1.57, p=0.049). The percentage of low HDL cholesterol values among Ranch Hands in the background dioxin category was 8.8 percent versus 7.4 percent for Comparisons.

The unadjusted Model 4 analysis showed nonsignificant results (Table 13-27(g): p=0.349). After covariate adjustment, a significant inverse relation between HDL cholesterol and 1987 dioxin level was shown (Table 13-27(h): Adj. RR=0.82, p=0.029). The percentages of low HDL cholesterol values in the low, medium, and high 1987 dioxin categories were 8.1, 9.5, and 7.4, respectively.

13.2.2.3.18 Cholesterol-HDL Ratio (Continuous)

The unadjusted Model 1 analysis of the cholesterol-HDL ratio did not disclose a significant difference between Ranch Hands and Comparisons (Table 13-28(a): p>0.15 for all contrasts). The adjusted analysis showed no significant difference between Ranch Hands and Comparisons combined across all occupations. Stratifying the analysis by occupation revealed a marginally significant group difference for the enlisted flyers (Table 13-28(b): difference of adjusted means=–0.27, p=0.051). Within the enlisted flyer stratum, the mean cholesterol-HDL ratio was lower for the Ranch Hands than for the Comparisons (4.49 versus 4.76).

Table 13-28. Analysis of Cholesterol-HDL Ratio (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***858***	***4.66***	***–0.02 --***	***0.723***
	Comparison	***1,230***	***4.68***		
Officer	Ranch Hand	340	4.39	–0.07 --	0.425
	Comparison	489	4.46		
Enlisted Flyer	Ranch Hand	149	4.72	–0.21 --	0.155
	Comparison	185	4.93		
Enlisted Groundcrew	Ranch Hand	369	4.90	0.10 --	0.282
	Comparison	556	4.81		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 13-28. Analysis of Cholesterol-HDL Ratio (Continuous) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***853***	***4.48***	***–0.03 --***	***0.546***
	Comparison	***1,228***	***4.51***		
Officer	Ranch Hand	340	4.21	–0.06 --	0.446
	Comparison	488	4.27		
Enlisted Flyer	Ranch Hand	147	4.49	–0.27 --	0.051
	Comparison	184	4.76		
Enlisted Groundcrew	Ranch Hand	366	4.67	0.08 --	0.316
	Comparison	556	4.58		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	157	4.52	4.55	0.055	0.028 (0.009)	0.003
Medium	159	4.92	4.93			
High	159	4.99	4.96			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of cholesterol-HDL ratio versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	157	4.49	0.118	0.007 (0.011)	0.499
Medium	158	4.77			
High	157	4.66			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of cholesterol-HDL ratio versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 13-28. Analysis of Cholesterol-HDL Ratio (Continuous) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	**n**	**Mean[a]**	**Adj. Mean[ab]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]**	**p-Value[d]**
Comparison	1,193	4.69	4.69		
Background RH	376	4.49	4.55	–0.14 --	0.068
Low RH	235	4.60	4.58	–0.11 --	0.220
High RH	240	5.02	4.95	0.26 --	0.005
Low plus High RH	475	4.81	4.76	0.07 --	0.282

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	**n**	**Adj. Mean[a]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]**	**p-Value[c]**
Comparison	1,192	4.52		
Background RH	374	4.45	–0.07 --	0.352
Low RH	234	4.43	–0.09 --	0.289
High RH	238	4.61	0.09 --	0.290
Low plus High RH	472	4.52	0.00 --	0.978

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin +1)**		
1987 Dioxin	**n**	**Mean[a]**	**R^2**	**Adjusted Slope (Std. Error)[b]**	**p-Value**
Low	283	4.44	0.030	0.033 (0.007)	<0.001
Medium	284	4.59			
High	284	4.97			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of cholesterol-HDL ratio versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 13-28. Analysis of Cholesterol-HDL Ratio (Continuous) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	4.34	0.074	0.021 (0.007)	0.006
Medium	282	4.44			
High	281	4.65			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of cholesterol-HDL ratio versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

A significant association between initial dioxin and the cholesterol-HDL ratio was seen in the Model 2 unadjusted analysis (Table 13-28(c): slope=0.028, p=0.003). The adjusted analysis results were nonsignificant (Table 13-28(d): p=0.499).

The unadjusted Model 3 analysis revealed significant differences between Ranch Hands in the background category and Comparisons, as well as between Ranch Hands in the high dioxin category and Comparisons (Table 13-28(e): difference of means=–0.14, p=0.068; difference of means=0.26, p=0.005, respectively). The adjusted Model 3 analysis did not show any of the Ranch Hand categories to be significantly different from the Comparison group (Table 13-28(f): p>0.28 for each analysis).

Both the unadjusted and adjusted Model 4 analyses revealed significant positive associations between 1987 dioxin and the cholesterol-HDL ratio (Table 13-28(g,h): slope=0.033, p<0.001, for unadjusted analysis; adjusted slope=0.021, p=0.006, for adjusted analysis). The mean cholesterol-HDL ratio values after covariate adjustment in the low, medium, and high 1987 dioxin categories were 4.34, 4.44, and 4.65, respectively.

13.2.2.3.19 Cholesterol-HDL Ratio (Discrete)

The unadjusted Model 1 analysis of the cholesterol-HDL ratio in its dichotomized form did not reveal a significant difference between Ranch Hands and Comparisons overall or stratified by occupation (Table 13-29(a): p>0.13 for all unadjusted contrasts). No significant overall group difference was found between all Ranch Hands and Comparisons in the adjusted analysis. After stratifying the adjusted analysis by occupation, a marginally significant group difference among the enlisted flyers was revealed (Table 13-29(b): Adj. RR=0.67, p=0.075). The percentage of Ranch Hand enlisted flyers with high cholesterol-HDL ratios was 38.9 percent versus 47.0 percent for Comparison enlisted flyers.

Table 13-29. Analysis of Cholesterol-HDL Ratio (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***858***	***356 (41.5)***	***1.02 (0.85,1.22)***	***0.843***
	Comparison	***1,230***	***505 (41.1)***		
Officer	Ranch Hand	340	114 (33.5)	1.08 (0.80,1.45)	0.623
	Comparison	489	156 (31.9)		
Enlisted Flyer	Ranch Hand	149	58 (38.9)	0.72 (0.46,1.11)	0.138
	Comparison	185	87 (47.0)		
Enlisted Groundcrew	Ranch Hand	369	184 (49.9)	1.12 (0.86,1.45)	0.414
	Comparison	556	262 (47.1)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.01 (0.85,1.22)***	***0.878***
Officer	1.09 (0.81,1.47)	0.563
Enlisted Flyer	0.67 (0.43,1.04)	0.075
Enlisted Groundcrew	1.11 (0.85,1.45)	0.436

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	157	54 (34.4)	1.25 (1.09,1.45)	0.002
Medium	159	77 (48.4)		
High	159	85 (53.5)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
472	1.08 (0.91,1.28)	0.378

[a] Relative risk for a twofold increase in initial dioxin.

Table 13-29. Analysis of Cholesterol-HDL Ratio (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,193	492 (41.2)		
Background RH	376	136 (36.2)	0.88 (0.69,1.13)	0.321
Low RH	235	86 (36.6)	0.80 (0.60,1.07)	0.135
High RH	240	130 (54.2)	1.57 (1.18,2.08)	0.002
Low plus High RH	475	216 (45.5)	1.12 (0.90,1.40)	0.295

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,192		
Background RH	374	1.00 (0.77,1.28)	0.982
Low RH	234	0.83 (0.61,1.12)	0.221
High RH	238	1.26 (0.93,1.69)	0.133
Low plus High RH	472	1.02 (0.82,1.28)	0.849

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	283	104 (36.7)	1.22 (1.11,1.34)	<0.001
Medium	284	98 (34.5)		
High	284	150 (52.8)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 13-29. Analysis of Cholesterol-HDL Ratio (Discrete) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
846	1.13 (1.01,1.26)	0.025

[a] Relative risk for a twofold increase in 1987 dioxin.

A significant positive association between the cholesterol-HDL ratio and initial dioxin was shown in the unadjusted Model 2 analysis (Table 13-29(c): Est. RR=1.25, p=0.002). After adjustment for covariates, the analysis results were nonsignificant (Table 13-29(d): p=0.378).

The Model 3 unadjusted analysis of the cholesterol-HDL ratio revealed a significant difference between Ranch Hands in the high dioxin category and Comparisons (Table 13-29(e): Est. RR=1.57, p=0.002). All contrasts between the Ranch Hand categories and Comparisons were nonsignificant in the adjusted analysis (Table 13-29(f): p>0.13 for each contrast).

The unadjusted and adjusted Model 4 analyses each revealed a significant relation between 1987 dioxin and cholesterol-HDL ratio (Table 13-29(g,h): Est. RR=1.22, p<0.001, for the unadjusted analysis; Adj. RR=1.13, p=0.025, for the adjusted analysis). The percentages of participants with high cholesterol-HDL ratios in the low, medium, and high 1987 dioxin categories were 36.7, 34.5, and 52.8, respectively.

13.2.2.3.20 Triglycerides (Continuous)

No significant associations with dioxin were shown in all Model 1 and 2 analyses (Table 13-30(a–d): p>0.10 for each analysis).

The unadjusted Model 3 analysis showed a significant difference between Ranch Hands in the high dioxin category and Comparisons, as well as between Ranch Hands in the low and high dioxin categories combined and Comparisons (Table 13-30(e): difference of means=20.1 mg/dl, p<0.001; difference of means=9.4 mg/dl, p=0.023, respectively).

Table 13-30. Analysis of Triglycerides (mg/dl) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***858***	***122.8***	***2.1 --***	***0.539***
	Comparison	***1,231***	***120.7***		
Officer	Ranch Hand	339	114.9	3.2 --	0.523
	Comparison	490	111.7		
Enlisted Flyer	Ranch Hand	150	123.9	−13.8 --	0.122
	Comparison	185	137.7		
Enlisted Groundcrew	Ranch Hand	369	130.0	6.4 --	0.230
	Comparison	556	123.6		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 13-30. Analysis of Triglycerides (mg/dl) (Continuous) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***853***	***107.4***	***1.8 --***	***0.546***
	Comparison	***1,229***	***105.6***		
Officer	Ranch Hand	339	100.3	3.2 --	0.458
	Comparison	489	97.1		
Enlisted Flyer	Ranch Hand	148	107.0	−12.4 --	0.109
	Comparison	184	119.5		
Enlisted Groundcrew	Ranch Hand	366	110.5	5.3 --	0.239
	Comparison	556	105.2		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	158	117.3	118.6	0.025	0.033 (0.023)	0.140
Medium	159	141.9	142.0			
High	159	141.0	139.4			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of triglycerides versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	158	106.9	0.055	0.006 (0.027)	0.830
Medium	158	123.9			
High	157	118.4			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of triglycerides versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 13-30. Analysis of Triglycerides (mg/dl) (Continuous) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	**n**	**Mean[a]**	**Adj. Mean[ab]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]**	**p-Value[d]**
Comparison	1,194	120.6	120.3		
Background RH	375	110.3	114.5	–5.8 --	0.172
Low RH	236	121.0	119.7	–0.6 --	0.897
High RH	240	145.8	140.4	20.1 --	<0.001
Low plus High RH	476	132.9	129.7	9.4 --	0.023

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	**n**	**Adj. Mean[a]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]**	**p-Value[c]**
Comparison	1,193	105.9		
Background RH	373	103.2	–2.7 --	0.483
Low RH	235	107.0	1.1 --	0.820
High RH	238	118.2	12.3 --	0.013
Low plus High RH	473	112.5	6.6 --	0.070

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin +1)**		
1987 Dioxin	**n**	**Mean[a]**	**R^2**	**Adjusted Slope (Std. Error)[b]**	**p-Value**
Low	282	109.2	0.028	0.072 (0.015)	<0.001
Medium	285	118.3			
High	284	141.9			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of triglycerides versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 13-30. Analysis of Triglycerides (mg/dl) (Continuous) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**		
1987 Dioxin	**n**	**Adj. Mean[a]**	**R^2**	**Adjusted Slope (Std. Error)[b]**	**p-Value**
Low	282	96.3	0.041	0.063 (0.017)	<0.001
Medium	283	105.7			
High	281	122.9			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of triglycerides versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

The adjusted Model 3 analysis of triglycerides revealed the same two significant contrasts: Ranch Hands in the high dioxin category versus Comparisons (Table 13-30(f): difference of adjusted means=12.3 mg/dl, p=0.013) and Ranch Hands in the low and high dioxin categories combined versus Comparisons (difference of adjusted means=6.6 mg/dl, p=0.070). The adjusted mean levels of triglycerides for Ranch Hands in the high dioxin category, Ranch Hands in the low and high dioxin categories combined, and Comparisons were 118.2 mg/dl, 112.5 mg/dl, and 105.9 mg/dl, respectively.

The Model 4 unadjusted and adjusted analyses both showed significant relations between 1987 dioxin and triglycerides (Table 13-30(g,h): slope=0.072, p<0.001, for the unadjusted analysis; adjusted slope=0.063, p<0.001, for the adjusted analysis). The adjusted mean triglyceride levels in the low, medium, and high 1987 dioxin categories were 96.3 mg/dl, 105.7 mg/dl, and 122.9 mg/dl, respectively.

13.2.2.3.21 Triglycerides (Discrete)

The unadjusted and adjusted Model 1 analyses of triglycerides in their discrete form showed no overall group differences (Table 13-31(a,b): p>0.31 for each analysis). After stratifying by occupation, significant group differences were noted within the enlisted groundcrew stratum for both the unadjusted and adjusted analyses (Table 13-31(a,b): Est. RR=1.36, p=0.052; Adj. RR=1.37, p=0.047, respectively). Among the enlisted groundcrew, 26.6 percent of the Ranch Hands had high triglyceride levels versus 21.0 percent of the Comparisons.

Table 13-31. Analysis of Triglycerides (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	**Group**	**n**	**Number (%) High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***858***	***188 (21.9)***	***1.10 (0.89,1.36)***	***0.377***
	Comparison	***1,231***	***250 (20.3)***		
Officer	Ranch Hand	339	60 (17.7)	1.07 (0.74,1.54)	0.717
	Comparison	490	82 (16.7)		
Enlisted Flyer	Ranch Hand	150	30 (20.0)	0.66 (0.39,1.10)	0.109
	Comparison	185	51 (27.6)		
Enlisted Groundcrew	Ranch Hand	369	98 (26.6)	1.36 (1.00,1.85)	0.052
	Comparison	556	117 (21.0)		

Table 13-31. Analysis of Triglycerides (Discrete) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.12 (0.90,1.39)***	***0.318***
Officer	1.10 (0.76,1.58)	0.628
Enlisted Flyer	0.66 (0.39,1.12)	0.123
Enlisted Groundcrew	1.37 (1.00,1.88)	0.047

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	158	37 (23.4)	1.09 (0.94,1.27)	0.275
Medium	159	45 (28.3)		
High	159	49 (30.8)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
473	0.96 (0.80,1.15)	0.690

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,194	240 (20.1)		
Background RH	375	53 (14.1)	0.72 (0.52,1.00)	0.051
Low RH	236	54 (22.9)	1.15 (0.82,1.62)	0.411
High RH	240	77 (32.1)	1.74 (1.27,2.37)	<0.001
Low plus High RH	476	131 (27.5)	1.42 (1.10,1.82)	0.006

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 13-31. Analysis of Triglycerides (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,193		
Background RH	373	0.79 (0.56,1.10)	0.161
Low RH	235	1.24 (0.88,1.76)	0.215
High RH	238	1.55 (1.12,2.15)	0.009
Low plus High RH	473	1.39 (1.07,1.80)	0.012

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	282	41 (14.5)	1.29 (1.16,1.44)	<0.001
Medium	285	58 (20.4)		
High	284	85 (29.9)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
846	1.23 (1.09,1.40)	0.001

[a] Relative risk for a twofold increase in 1987 dioxin.

The Model 2 unadjusted and adjusted analyses showed no significant association between initial dioxin and triglycerides (Table 13-31(c,d): p>0.27 for each analysis). The unadjusted Model 3 analysis of triglycerides revealed Ranch Hands in the background dioxin category, Ranch Hands in the high dioxin category, and Ranch Hands in the low and high dioxin categories combined each to be significantly different from the Comparisons (Table 13-31(e): Est. RR=0.72, p=0.051, for the background dioxin category contrast; Est. RR=1.74, p<0.001, for the high dioxin category contrast; and Est. RR=1.42, p=0.006, for the low and high dioxin categories combined contrast). The adjusted Model 3 analysis showed a significant difference between Ranch Hands in the high dioxin category and Comparisons (Table 13-31(f): Adj. RR=1.55, p=0.009), as well as a significant difference between Ranch Hands in the low and high dioxin categories combined and Comparisons (Adj. RR=1.39, p=0.012). The percentages of individuals with high triglyceride levels among Ranch Hands in the high dioxin category, Ranch Hands in the low and high dioxin categories combined, and Comparisons were 32.1, 27.5, and 20.1, respectively.

The unadjusted and adjusted Model 4 analyses each revealed a significant association between triglycerides and 1987 dioxin levels (Table 13-31(g,h): Est. RR=1.29, p<0.001, for the unadjusted analysis; Adj. RR=1.23, p=0.001, for the adjusted analysis). The percentages of participants with high levels of triglycerides in the low, medium, and high 1987 dioxin categories were 14.5, 20.4, and 29.9, respectively.

13.2.2.3.22 Creatine Phosphokinase (Continuous)

All unadjusted and adjusted analyses in Models 1 through 3 showed no significant associations between dioxin and creatine phosphokinase (Table 13-32(a–f): p>0.50 for each analysis).

Table 13-32. Analysis of Creatine Phosphokinase (U/l) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***859***	***106.3***	***0.8 --***	***0.791***
	Comparison	***1,231***	***105.5***		
Officer	Ranch Hand	340	105.8	1.4 --	0.748
	Comparison	490	104.3		
Enlisted Flyer	Ranch Hand	150	97.2	–3.8 --	0.562
	Comparison	185	101.0		
Enlisted Groundcrew	Ranch Hand	369	110.8	2.6 --	0.565
	Comparison	556	108.2		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***854***	***140.3***	***0.9 --***	***0.809***
	Comparison	***1,229***	***139.4***		
Officer	Ranch Hand	340	147.7	2.4 --	0.696
	Comparison	489	145.3		
Enlisted Flyer	Ranch Hand	148	131.5	–4.9 --	0.568
	Comparison	184	136.4		
Enlisted Groundcrew	Ranch Hand	366	140.2	1.8 --	0.736
	Comparison	556	138.3		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 13-32. Analysis of Creatine Phosphokinase (U/l) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	158	111.8	112.7	0.013	0.005 (0.021)	0.800
Medium	159	104.0	104.1			
High	159	112.0	111.1			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of creatine phosphokinase versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	158	149.8	0.121	–0.004 (0.023)	0.871
Medium	158	139.9			
High	157	143.6			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of creatine phosphokinase versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,194	105.6	105.4		
Background RH	376	102.7	105.6	0.2 --	0.961
Low RH	236	109.1	108.2	2.8 --	0.547
High RH	240	109.3	106.3	0.9 --	0.843
Low plus High RH	476	109.2	107.2	1.8 --	0.602

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 13-32. Analysis of Creatine Phosphokinase (U/l) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,193	140.2		
Background RH	374	139.5	–0.7 --	0.889
Low RH	235	142.6	2.4 --	0.679
High RH	238	143.8	3.6 --	0.549
Low plus High RH	473	143.2	3.0 --	0.503

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	99.8	0.004	0.024 (0.014)	0.084
Medium	285	110.6			
High	284	108.7			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of creatine phosphokinase versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	126.6	0.091	0.039 (0.015)	0.011
Medium	283	141.1			
High	281	143.2			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of creatine phosphokinase versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

The unadjusted and adjusted Model 4 analyses each showed a positive relation between 1987 dioxin and creatine phosphokinase, with the unadjusted slope marginally significant and the adjusted slope significant (Table 13-32(g,h): slope=0.024, p=0.084; adjusted slope=0.039, p=0.011). The adjusted mean creatine phosphokinase levels in the low, medium, and high 1987 dioxin categories were 126.6 U/l, 141.1 U/l, and 143.2 U/l, respectively.

13.2.2.3.23 Creatine Phosphokinase (Discrete)

All analyses of high creatine phosphokinase levels in Models 1 through 3 were nonsignificant (Table 13-33(a–f): p≥0.21 for each analysis).

Table 13-33. Analysis of Creatine Phosphokinase (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***72 (8.4)***	***0.89 (0.65,1.21)***	***0.448***
	Comparison	***1,231***	***115 (9.3)***		
Officer	Ranch Hand	340	26 (7.6)	0.84 (0.51,1.39)	0.497
	Comparison	490	44 (9.0)		
Enlisted Flyer	Ranch Hand	150	7 (4.7)	0.55 (0.22,1.40)	0.212
	Comparison	185	15 (8.1)		
Enlisted Groundcrew	Ranch Hand	369	39 (10.6)	1.06 (0.69,1.62)	0.807
	Comparison	556	56 (10.1)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.87 (0.63,1.20)***	***0.390***
Officer	0.84 (0.50,1.41)	0.519
Enlisted Flyer	0.55 (0.21,1.41)	0.210
Enlisted Groundcrew	1.00 (0.63,1.58)	0.998

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	158	16 (10.1)	1.05 (0.83,1.32)	0.698
Medium	159	12 (7.5)		
High	159	17 (10.7)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
473	1.09 (0.82,1.45)	0.542

[a] Relative risk for a twofold increase in initial dioxin.

Table 13-33. Analysis of Creatine Phosphokinase (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,194	111 (9.3)		
Background RH	376	26 (6.9)	0.81 (0.51,1.26)	0.345
Low RH	236	20 (8.5)	0.87 (0.53,1.44)	0.599
High RH	240	25 (10.4)	1.03 (0.65,1.64)	0.905
Low plus High RH	476	45 (9.5)	0.95 (0.66,1.37)	0.781

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,193		
Background RH	374	0.75 (0.46,1.20)	0.227
Low RH	235	0.80 (0.47,1.35)	0.402
High RH	238	1.20 (0.73,1.98)	0.465
Low plus High RH	473	0.98 (0.67,1.45)	0.923

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	283	17 (6.0)	1.14 (0.97,1.33)	0.123
Medium	285	26 (9.1)		
High	284	28 (9.9)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
847	1.22 (1.00,1.49)	0.043

[a] Relative risk for a twofold increase in 1987 dioxin.

The unadjusted Model 4 analysis results were nonsignificant (Table 13-33(g): p=0.123). After adjusting for covariates, a significant relation between creatine phosphokinase in its dichotomous form and 1987 dioxin was revealed (Table 13-33(h): Adj. RR=1.22, p=0.043). The percentages of participants with high levels of creatine phosphokinase in the low, medium, and high 1987 dioxin categories were 6.0, 9.1, and 9.9, respectively.

13.2.2.3.24 Serum Amylase (Continuous)

The unadjusted and adjusted Model 1 analyses of serum amylase did not show a significant overall group difference between Ranch Hands and Comparisons (Table 13-34(a,b): p>0.92 for each analysis). Stratifying the analyses by occupation revealed a significant group difference among the officers in both the unadjusted and adjusted analyses (Table 13-34(a,b): difference of means=–2.98 U/l, p=0.048, for the unadjusted analysis; difference of adjusted means=–3.50 U/l, p=0.037, for the adjusted analysis). The adjusted mean serum amylase level among the officers in the Ranch Hand group was 61.86 U/l versus 65.36 U/l among the officers in the Comparison group.

The results from the unadjusted Model 2 analysis revealed a marginally significant inverse association between serum amylase and initial dioxin (Table 13-34(c): slope=–0.024, p=0.070). Similarly, after covariate adjustment, a marginally significant inverse association between serum amylase and initial dioxin was present (Table 13-34(d): adjusted slope=–0.029, p=0.060). The adjusted mean serum amylase levels in the low, medium, and high initial dioxin categories were 67.45 U/l, 64.22 U/l, and 64.25 U/l, respectively.

Table 13-34. Analysis of Serum Amylase (U/l) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***859***	***56.92***	***0.07 --***	***0.942***
	Comparison	***1,231***	***56.85***		
Officer	Ranch Hand	340	54.88	–2.98 --	0.048
	Comparison	490	57.86		
Enlisted Flyer	Ranch Hand	150	58.46	2.55 --	0.284
	Comparison	185	55.91		
Enlisted Groundcrew	Ranch Hand	369	58.23	1.95 --	0.182
	Comparison	556	56.29		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 13-34. Analysis of Serum Amylase (U/l) (Continuous) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***854***	***63.65***	***–0.09 --***	***0.929***
	Comparison	***1,229***	***63.74***		
Officer	Ranch Hand	340	61.86	–3.50 --	0.037
	Comparison	489	65.36		
Enlisted Flyer	Ranch Hand	148	65.17	2.73 --	0.301
	Comparison	184	62.44		
Enlisted Groundcrew	Ranch Hand	366	64.84	1.98 --	0.218
	Comparison	556	62.86		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	158	59.22	58.66	0.052	–0.024 (0.013)	0.070
Medium	159	55.89	55.83			
High	159	55.54	56.13			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of serum amylase versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	158	67.45	0.125	–0.029 (0.015)	0.060
Medium	158	64.22			
High	157	64.25			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of serum amylase versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 13-34. Analysis of Serum Amylase (U/l) (Continuous) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,194	56.82	56.88		
Background RH	376	57.03	55.87	−1.01 --	0.419
Low RH	236	60.17	60.54	3.66 --	0.019
High RH	240	53.78	54.89	−1.99 --	0.178
Low plus High RH	476	56.86	57.63	0.75 --	0.523

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,193	63.45		
Background RH	374	62.33	−1.12 --	0.427
Low RH	235	66.45	3.00 --	0.078
High RH	238	61.31	−2.14 --	0.205
Low plus High RH	473	63.82	0.37 --	0.774

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 13-34. Analysis of Serum Amylase (U/l) (Continuous) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	57.84	0.005	–0.019 (0.009)	0.035
Medium	285	57.77			
High	284	55.23			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of serum amylase versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	68.24	0.063	–0.030 (0.010)	0.003
Medium	283	66.40			
High	281	62.16			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of serum amylase versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

The unadjusted Model 3 analysis revealed a significant difference in mean serum amylase levels between Ranch Hands in the low dioxin category and Comparisons (Table 13-34(e): difference of means=3.66 U/l, p=0.019). The adjusted results showed a marginally significant difference between Ranch Hands in the low dioxin category and Comparisons (Table 13-34(f): difference of adjusted means=3.00 U/l, p=0.078). The adjusted mean serum amylase level for Ranch Hands in the low dioxin category was 66.45 U/l versus 63.45 U/l for Comparisons.

Both the unadjusted and adjusted Model 4 analyses showed serum amylase to be significantly inversely associated with 1987 dioxin (Table 13-34(g,h): slope=–0.019, p=0.035; adjusted slope=–0.030, p=0.003). The adjusted mean serum amylase levels in the low, medium, and high 1987 dioxin categories were 68.24 U/l, 66.40 U/l, and 62.16 U/l, respectively.

13.2.2.3.25 Serum Amylase (Discrete)

The unadjusted and adjusted Model 1 analyses revealed no significant overall group difference in the percentage of individuals with high serum amylase levels (Table 13-35(a,b): p>0.73 for each analysis). In both the unadjusted and adjusted analyses, stratifying by occupation revealed marginally significant reduction in risk among the Ranch Hand officers (Table 13-35(a,b): Est. RR=0.45, p=0.067, for the unadjusted analysis; Adj. RR=0.43, p=0.058, for the adjusted analysis). Among the officers in the Ranch Hand group, 2.1 percent had high serum amylase levels versus 4.5 percent of officers in the Comparison group. All analyses of Models 2, 3, and 4 showed no significant associations between serum amylase and dioxin (Table 13-35(c–h): p>0.11 for each analysis).

Table 13-35. Analysis of Serum Amylase (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***25 (2.9)***	***0.94 (0.56,1.57)***	***0.816***
	Comparison	***1,231***	***38 (3.1)***		
Officer	Ranch Hand	340	7 (2.1)	0.45 (0.19,1.06)	0.067
	Comparison	490	22 (4.5)		
Enlisted Flyer	Ranch Hand	150	4 (2.7)	1.66 (0.37,7.54)	0.510
	Comparison	185	3 (1.6)		
Enlisted Groundcrew	Ranch Hand	369	14 (3.8)	1.65 (0.77,3.55)	0.202
	Comparison	556	13 (2.3)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.91 (0.54,1.54)***	***0.733***
Officer	0.43 (0.18,1.03)	0.058
Enlisted Flyer	1.66 (0.36,7.69)	0.514
Enlisted Groundcrew	1.60 (0.73,3.50)	0.240

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	158	7 (4.4)	0.86 (0.58,1.29)	0.458
Medium	159	5 (3.1)		
High	159	5 (3.1)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
473	1.04 (0.63,1.71)	0.884

[a] Relative risk for a twofold increase in initial dioxin.

Table 13-35. Analysis of Serum Amylase (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	**n**	**Number (%) High**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,194	38 (3.2)		
Background RH	376	8 (2.1)	0.61 (0.28,1.32)	0.210
Low RH	236	11 (4.7)	1.51 (0.76,3.01)	0.236
High RH	240	6 (2.5)	0.84 (0.35,2.02)	0.697
Low plus High RH	476	17 (3.6)	1.13 (0.62,2.06)	0.701

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Comparison	1,193		
Background RH	374	0.53 (0.24,1.16)	0.112
Low RH	235	1.37 (0.67,2.77)	0.387
High RH	238	1.02 (0.41,2.59)	0.959
Low plus High RH	473	1.18 (0.63,2.21)	0.602

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**	
1987 Dioxin	**n**	**Number (%) High**	**Estimated Relative Risk (95% C.I.)[a]**	**p-Value**
Low	283	7 (2.5)	0.93 (0.70,1.22)	0.590
Medium	285	10 (3.5)		
High	284	8 (2.8)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 13-35. Analysis of Serum Amylase (Discrete) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
847	0.93 (0.68,1.26)	0.623

[a] Relative risk for a twofold increase in 1987 dioxin.

13.2.2.3.26 Antibodies for Hepatitis A

All unadjusted and adjusted analyses in Models 1 through 4 showed no significant associations between dioxin and the presence of antibodies for hepatitis A (Table 13-36(a–h): p>0.12 for each analysis).

Table 13-36. Analysis of Antibodies for Hepatitis A

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***870***	***283 (32.5)***	***0.95 (0.79,1.14)***	***0.580***
	Comparison	***1,250***	***421 (33.7)***		
Officer	Ranch Hand	341	92 (27.0)	1.00 (0.73,1.36)	0.999
	Comparison	493	133 (27.0)		
Enlisted Flyer	Ranch Hand	151	74 (49.0)	1.13 (0.73,1.73)	0.581
	Comparison	187	86 (46.0)		
Enlisted Groundcrew	Ranch Hand	378	117 (31.0)	0.82 (0.62,1.08)	0.153
	Comparison	570	202 (35.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.93 (0.76,1.12)***	***0.434***
Officer	0.95 (0.68,1.31)	0.739
Enlisted Flyer	1.07 (0.69,1.68)	0.754
Enlisted Groundcrew	0.85 (0.64,1.14)	0.285

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	57 (35.6)	0.98 (0.85,1.14)	0.830
Medium	162	54 (33.3)		
High	160	57 (35.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 13-36. Analysis of Antibodies for Hepatitis A (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log₂ (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
479	1.02 (0.86,1.22)	0.813

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,212	405 (33.4)		
Background RH	381	112 (29.4)	0.84 (0.65,1.08)	0.175
Low RH	239	84 (35.1)	1.08 (0.80,1.44)	0.619
High RH	243	84 (34.6)	1.04 (0.78,1.39)	0.784
Low plus High RH	482	168 (34.9)	1.06 (0.85,1.32)	0.615

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,211		
Background RH	378	0.92 (0.70,1.21)	0.561
Low RH	238	0.92 (0.67,1.25)	0.577
High RH	241	0.96 (0.70,1.32)	0.787
Low plus High RH	479	0.94 (0.74,1.19)	0.588

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log₂ (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	81 (28.1)	1.08 (0.98,1.19)	0.125
Medium	287	103 (35.9)		
High	288	96 (33.3)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 13-36. Analysis of Antibodies for Hepatitis A (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
857	1.06 (0.94,1.19)	0.346

[a] Relative risk for a twofold increase in 1987 dioxin.

13.2.2.3.27 Evidence of Prior Hepatitis B

The unadjusted Model 1 analysis of serological evidence of prior hepatitis B revealed a significant overall group difference between Ranch Hands and Comparisons (Table 13-37(a): Est. RR=0.62, p=0.001). After stratifying by occupation, a significant difference between Ranch Hands and Comparisons was seen within each occupational stratum (Table 13-37(a): Est. RR=0.49, p=0.031, for officers; Est. RR=0.58, p=0.079, for enlisted flyers; and Est. RR=0.66, p=0.035, for enlisted groundcrew). In each stratum, the percentage of participants with evidence of prior hepatitis B was greater for Comparisons than for Ranch Hands.

Table 13-37. Analysis of Evidence of Prior Hepatitis B

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***869***	***77 (8.9)***	***0.62 (0.46,0.82)***	***0.001***
	Comparison	***1,249***	***170 (13.6)***		
Officer	Ranch Hand	340	13 (3.8)	0.49 (0.26,0.94)	0.031
	Comparison	494	37 (7.5)		
Enlisted Flyer	Ranch Hand	151	19 (12.6)	0.58 (0.32,1.06)	0.079
	Comparison	187	37 (19.8)		
Enlisted Groundcrew	Ranch Hand	378	45 (11.9)	0.66 (0.45,0.97)	0.035
	Comparison	568	96 (16.9)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.59 (0.44,0.80)***	***<0.001***
Officer	0.47 (0.25,0.91)	0.024
Enlisted Flyer	0.58 (0.31,1.07)	0.079
Enlisted Groundcrew	0.66 (0.44,0.97)	0.035

Table 13-37. Analysis of Evidence of Prior Hepatitis B (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	159	17 (10.7)	1.06 (0.86,1.31)	0.588
Medium	162	14 (8.6)		
High	160	22 (13.8)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
478	0.95 (0.74,1.22)	0.669

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	166 (13.7)		
Background RH	381	23 (6.0)	0.42 (0.27,0.66)	<0.001
Low RH	238	26 (10.9)	0.76 (0.49,1.18)	0.229
High RH	243	27 (11.1)	0.76 (0.49,1.17)	0.214
Low plus High RH	481	53 (11.0)	0.76 (0.55,1.06)	0.105

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,210		
Background RH	378	0.50 (0.31,0.80)	0.004
Low RH	237	0.71 (0.45,1.12)	0.143
High RH	241	0.59 (0.37,0.92)	0.021
Low plus High RH	478	0.65 (0.46,0.91)	0.012

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 13-37. Analysis of Evidence of Prior Hepatitis B (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	14 (4.9)	1.20 (1.03,1.40)	0.023
Medium	286	27 (9.4)		
High	288	35 (12.2)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
856	1.06 (0.89,1.25)	0.531

[a] Relative risk for a twofold increase in 1987 dioxin.

The adjusted Model 1 analysis mirrored the unadjusted analysis. Significant differences were seen between all Ranch Hands and Comparisons (Table 13-37(b): Adj. RR=0.59, p<0.001) and within each occupational stratum (Table 13-37(b): Adj. RR=0.47, p=0.024, for officers; Adj. RR=0.58, p=0.079, for enlisted flyers; and Adj. RR=0.66, p=0.035, for enlisted groundcrew). Both the unadjusted and adjusted Model 2 analyses revealed no relation between prior hepatitis B and initial dioxin (Table 13-37(c,d): p>0.58 for each analysis).

The unadjusted Model 3 analysis revealed a significant difference in prior hepatitis B between Ranch Hands in the background dioxin category and Comparisons (Table 13-37(e): Est. RR=0.42, p<0.001). The adjusted results showed a significant difference between Ranch Hands in the background dioxin category and Comparisons (Table 13-37(f): Adj. RR=0.50, p=0.004), as well as differences between Ranch Hands in the high dioxin category and Comparisons and Ranch Hands in the low and high dioxin categories combined and Comparisons (Table 13-37(f): Adj. RR=0.59, p=0.021; Adj. RR=0.65, p=0.012, respectively). The percentages of participants with evidence of prior hepatitis B were 6.0 in the background dioxin category, 11.1 in the high dioxin category, 11.0 in the low and high dioxin categories combined, and 13.7 in the Comparison category.

The unadjusted Model 4 analysis revealed a significant relation between evidence of prior hepatitis B and 1987 dioxin (Table 13-37(g): Est. RR=1.20, p=0.023). After adjusting for covariates, the relation became nonsignificant (Table 13-37(h): p=0.531).

13.2.2.3.28 Current Hepatitis B

All unadjusted and adjusted analyses of current hepatitis B for Models 1 through 4 were nonsignificant (Table 13-38(a,b): p>0.45 for each analysis).

Table 13-38. Analysis of Current Hepatitis B

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***870***	***1 (0.1)***	***0.72 (0.07,7.94)***	***0.784***
	Comparison	***1,251***	***2 (0.2)***		
Officer	Ranch Hand	341	0 (0.0)	--	--
	Comparison	494	0 (0.0)		
Enlisted Flyer	Ranch Hand	151	0 (0.0)	--	--
	Comparison	187	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	378	1 (0.3)	0.75 (0.07,8.34)	0.817
	Comparison	570	2 (0.4)		

--: Results not presented because of the sparse number of participants with current hepatitis B.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.56 (0.05,6.93)***	***0.646***
Officer	--	--
Enlisted Flyer	--	--
Enlisted Groundcrew	0.68 (0.06,8.27)	0.762

--: Results not presented because of the sparse number of participants with current hepatitis B.

Note: Results for analysis across all occupational categories are not adjusted for occupation because of the sparse number of participants with current hepatitis B.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	0 (0.0)	0.99 (0.17,5.76)	0.987
Medium	162	1 (0.6)		
High	160	0 (0.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
479	0.39 (0.02,9.42)	0.497

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are adjusted only for percent body fat at the time of the blood measurement of dioxin, age, and lifetime alcohol history because of the sparse number of Ranch Hands with current hepatitis B.

Table 13-38. Analysis of Current Hepatitis B (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,213	2 (0.2)		
Background RH	381	0 (0.0)	--	0.999[c]
Low RH	239	1 (0.4)	2.52 (0.23,27.92)	0.453
High RH	243	0 (0.0)	--	0.999[c]
Low plus High RH	482	1 (0.2)	--	0.999[c]

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] P-value determined using a chi-square test with continuity correction because of the sparse number of Ranch Hands with current hepatitis B.
--: Results not presented because of the sparse number of Ranch Hands with current hepatitis B.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,212		
Background RH	378	--	--
Low RH	238	1.94 (0.14,26.64)	0.622
High RH	241	--	--
Low plus High RH	479	--	--

[a] Relative risk and confidence interval relative to Comparisons.
--: Results not presented because of the sparse number of Ranch Hands with current hepatitis B.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for occupation because of the sparse number of Ranch Hands with current hepatitis B.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	0 (0.0)	1.37 (0.41,4.55)	0.617
Medium	287	0 (0.0)		
High	288	1 (0.3)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 13-38. Analysis of Current Hepatitis B (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
857	1.33 (0.27,6.59)[b]	0.719

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race, occupation, industrial chemical exposure, and degreasing chemical exposure because of the sparse number of Ranch Hands with current hepatitis B.

13.2.2.3.29 Antibodies for Hepatitis C

No significant associations were seen between dioxin and hepatitis C for all unadjusted and adjusted analyses in Models 1 through 4 (Table 13-39(a–h): p>0.13).

Table 13-39. Analysis of Antibodies for Hepatitis C

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***870***	***9 (1.0)***	***0.72 (0.32,1.60)***	***0.408***
	Comparison	***1,251***	***18 (1.4)***		
Officer	Ranch Hand	341	1 (0.3)	0.36 (0.04,3.24)	0.362
	Comparison	494	4 (0.8)		
Enlisted Flyer	Ranch Hand	151	1 (0.7)	0.62 (0.06,6.87)	0.694
	Comparison	187	2 (1.1)		
Enlisted Groundcrew	Ranch Hand	378	7 (1.9)	0.88 (0.34,2.25)	0.785
	Comparison	570	12 (2.1)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.63 (0.27,1.47)***	***0.274***
Officer	0.36 (0.04,3.27)	0.367
Enlisted Flyer	0.61 (0.05,6.87)	0.690
Enlisted Groundcrew	0.73 (0.27,1.98)	0.532

Table 13-39. Analysis of Antibodies for Hepatitis C (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	2 (1.3)	0.61 (0.24,1.60)	0.271
Medium	162	2 (1.2)		
High	160	0 (0.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
479	0.63 (0.23,1.75)	0.344

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for occupation, industrial chemical exposure, and degreasing chemical exposure because of the sparse number of Ranch Hands with antibodies for hepatitis C.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,213	17 (1.4)		
Background RH	381	5 (1.3)	0.89 (0.32,2.44)	0.819
Low RH	239	2 (0.8)	0.60 (0.14,2.62)	0.497
High RH	243	2 (0.8)	0.61 (0.14,2.67)	0.512
Low plus High RH	482	4 (0.8)	0.61 (0.20,1.81)	0.369

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 13-39. Analysis of Antibodies for Hepatitis C (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,212		
Background RH	378	0.87 (0.28,2.73)	0.816
Low RH	238	0.54 (0.12,2.40)	0.415
High RH	241	0.50 (0.11,2.23)	0.359
Low plus High RH	479	0.52 (0.17,1.57)	0.243

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	5 (1.7)	0.69 (0.42,1.14)	0.139
Medium	287	2 (0.7)		
High	288	2 (0.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
857	0.67 (0.40,1.14)	0.141

[a] Relative risk for a twofold increase in 1987 dioxin.

13.2.2.3.30 Antibodies for Hepatitis D

Only one participant had positive results for hepatitis D antibodies. He was a Black Ranch Hand in the enlisted groundcrew occupational stratum. No further analyses were performed.

13.2.2.3.31 Stool Hemoccult

All unadjusted and adjusted analyses of stool hemoccult for Models 1 through 4 were nonsignificant (Table 13-40(a–h): p>0.17 for each analysis).

Table 13-40. Analysis of Stool Hemoccult

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***834***	***29 (3.5)***	***0.78 (0.49,1.23)***	***0.279***
	Comparison	***1,196***	***53 (4.4)***		
Officer	Ranch Hand	332	14 (4.2)	0.92 (0.46,1.83)	0.818
	Comparison	483	22 (4.6)		
Enlisted Flyer	Ranch Hand	147	2 (1.4)	0.34 (0.07,1.65)	0.179
	Comparison	178	7 (3.9)		
Enlisted Groundcrew	Ranch Hand	355	13 (3.7)	0.81 (0.41,1.61)	0.547
	Comparison	535	24 (4.5)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.78 (0.49,1.25)***	***0.301***
Officer	0.90 (0.45,1.80)	0.774
Enlisted Flyer	0.34 (0.07,1.70)	0.191
Enlisted Groundcrew	0.82 (0.41,1.64)	0.574

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	156	4 (2.6)	0.85 (0.59,1.24)	0.390
Medium	156	11 (7.1)		
High	152	4 (2.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
461	0.97 (0.62,1.51)	0.880

[a] Relative risk for a twofold increase in initial dioxin.

Table 13-40. Analysis of Stool Hemoccult (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,162	50 (4.3)		
Background RH	365	10 (2.7)	0.68 (0.34,1.35)	0.270
Low RH	232	11 (4.7)	1.08 (0.55,2.12)	0.814
High RH	232	8 (3.4)	0.74 (0.35,1.59)	0.443
Low plus High RH	464	19 (4.1)	0.90 (0.52,1.55)	0.696

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,161		
Background RH	363	0.63 (0.31,1.28)	0.201
Low RH	231	1.08 (0.55,2.13)	0.822
High RH	230	0.86 (0.39,1.90)	0.705
Low plus High RH	461	0.96 (0.55,1.68)	0.895

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	275	8 (2.9)	1.04 (0.81,1.34)	0.760
Medium	280	9 (3.2)		
High	274	12 (4.4)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 13-40. Analysis of Stool Hemoccult (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
824	1.13 (0.83,1.53)	0.448

[a] Relative risk for a twofold increase in 1987 dioxin.

13.2.2.3.32 Prealbumin (Continuous)

The unadjusted and adjusted analyses of prealbumin in its continuous form displayed no significant associations with dioxin in any of Models 1 through 4 (Table 13-41(a–h): p>0.38 for each analysis).

Table 13-41. Analysis of Prealbumin (mg/dl) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean	Difference of Means (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***29.54***	***–0.07 (–0.50,0.37)***	***0.766***
	Comparison	***1,231***	***29.61***		
Officer	Ranch Hand	340	29.65	–0.22 (–0.92,0.47)	0.532
	Comparison	490	29.87		
Enlisted Flyer	Ranch Hand	150	29.56	0.23 (–0.85,1.31)	0.679
	Comparison	185	29.33		
Enlisted Groundcrew	Ranch Hand	369	29.44	–0.03 (–0.70,0.63)	0.922
	Comparison	556	29.48		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adj. Mean	Difference of Adj. Means (95% C.I.)	p-Value
All	***Ranch Hand***	***854***	***29.66***	***–0.04 (–0.47,0.39)***	***0.861***
	Comparison	***1,229***	***29.70***		
Officer	Ranch Hand	340	30.03	–0.17 (–0.86,0.51)	0.621
	Comparison	489	30.20		
Enlisted Flyer	Ranch Hand	148	30.03	0.48 (–0.59,1.55)	0.382
	Comparison	184	29.55		
Enlisted Groundcrew	Ranch Hand	366	29.10	–0.11 (–0.76,0.54)	0.746
	Comparison	556	29.21		

Table 13-41. Analysis of Prealbumin (mg/dl) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Mean	Adj. Mean[a]	R^2	Slope (Std. Error)	p-Value
Low	158	29.72	29.61	0.030	–0.041 (0.178)	0.818
Medium	159	28.77	28.76			
High	159	29.83	29.95			

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean	R^2	Adj. Slope (Std. Error)	p-Value
Low	158	29.69	0.072	–0.127 (0.207)	0.538
Medium	158	28.68			
High	157	29.77			

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,194	29.61	29.62		
Background RH	376	29.72	29.53	–0.09 (–0.67,0.49)	0.760
Low RH	236	29.41	29.47	–0.15 (–0.85,0.54)	0.665
High RH	240	29.47	29.65	0.03 (–0.66,0.73)	0.927
Low plus High RH	476	29.44	29.56	–0.06 (–0.59,0.47)	0.825

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 13-41. Analysis of Prealbumin (mg/dl) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	**n**	**Adj. Mean**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)**	**p-Value**
Comparison	1,193	29.65		
Background RH	374	29.51	–0.15 (–0.73,0.44)	0.626
Low RH	235	29.69	0.04 (–0.65,0.73)	0.908
High RH	238	29.72	0.06 (–0.64,0.77)	0.860
Low plus High RH	473	29.71	0.05 (–0.48,0.58)	0.847

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin +1)**		
1987 Dioxin	**n**	**Mean**	**R^2**	**Adjusted Slope (Std. Error)**	**p-Value**
Low	283	30.00	<0.001	–0.047 (0.124)	0.704
Medium	285	29.28			
High	284	29.41			

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**		
1987 Dioxin	**n**	**Adj. Mean**	**R^2**	**Adjusted Slope (Std. Error)**	**p-Value**
Low	283	29.90	0.053	–0.007 (0.140)	0.961
Medium	283	29.43			
High	281	29.35			

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

13.2.2.3.33 Prealbumin (Discrete)

The unadjusted and adjusted Model 1 analyses did not disclose a significant overall difference in prealbumin levels between Ranch Hands and Comparisons (Table 13-42(a,b): p>0.13 for each analysis). After stratifying the unadjusted analysis by occupation, a marginally significant difference between Ranch Hands and Comparisons was noted among enlisted groundcrew (Table 13-42(a): Est. RR=3.56, p=0.067). Similarly, the stratified adjusted analysis revealed a significant difference between enlisted groundcrew Ranch Hands and enlisted groundcrew Comparisons (Table 13-42(b): Adj. RR=4.27, p=0.043). The percentage of Ranch Hand enlisted groundcrew with low prealbumin levels was 1.9 percent versus 0.5 percent of Comparison enlisted groundcrew.

Table 13-42. Analysis of Prealbumin (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Low	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***13 (1.5)***	***1.70 (0.76,3.82)***	***0.195***
	Comparison	***1,231***	***11 (0.9)***		
Officer	Ranch Hand	340	5 (1.5)	1.03 (0.32,3.27)	0.960
	Comparison	490	7 (1.4)		
Enlisted Flyer	Ranch Hand	150	1 (0.7)	1.23 (0.08,19.91)	0.882
	Comparison	185	1 (0.5)		
Enlisted Groundcrew	Ranch Hand	369	7 (1.9)	3.56 (0.92,13.87)	0.067
	Comparison	556	3 (0.5)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.87 (0.82,4.26)***	***0.136***
Officer	1.03 (0.32,3.29)	0.962
Enlisted Flyer	1.64 (0.09,28.94)	0.736
Enlisted Groundcrew	4.27 (1.05,17.39)	0.043

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Low	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	158	1 (0.6)	1.44 (0.84,2.47)	0.203
Medium	159	3 (1.9)		
High	159	2 (1.3)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
473	1.76 (0.94,3.30)	0.081

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for occupation because of the sparse number of Ranch Hands with low prealbumin levels.

Table 13-42. Analysis of Prealbumin (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	**n**	**Number (%) Low**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,194	10 (0.8)		
Background RH	376	6 (1.6)	1.94 (0.69,5.41)	0.207
Low RH	236	1 (0.4)	0.50 (0.06,3.95)	0.513
High RH	240	5 (2.1)	2.50 (0.84,7.42)	0.099
Low plus High RH	476	6 (1.3)	1.13 (0.33,3.90)	0.849

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Comparison	1,193		
Background RH	374	1.74 (0.61,5.01)	0.302
Low RH	235	0.49 (0.06,3.93)	0.506
High RH	238	4.34 (1.25,15.05)	0.021
Low plus High RH	473	1.48 (0.41,5.32)	0.552

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**	
1987 Dioxin	**n**	**Number (%) Low**	**Estimated Relative Risk (95% C.I.)[a]**	**p-Value**
Low	283	4 (1.4)	1.02 (0.69,1.49)	0.931
Medium	285	3 (1.1)		
High	284	5 (1.8)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 13-42. Analysis of Prealbumin (Discrete) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
847	1.00 (0.63,1.60)	0.993

[a] Relative risk for a twofold increase in 1987 dioxin.

No significant relation between prealbumin and initial dioxin was found in the unadjusted Model 2 analysis (Table 13-42(c): p=0.203). A marginally significant relation was found in the adjusted analysis (Table 13-42(d): Adj. RR=1.76, p=0.081), indicating an increased prevalence of low prealbumin levels as initial dioxin increased. In the Model 3 unadjusted analysis of prealbumin, a marginally significant difference was revealed between Ranch Hands in the high dioxin category and the Comparison group (Table 13-42(e): Est. RR=2.50, p=0.099). The same contrast was significant in the adjusted analysis (Table 13-42(f): Adj. RR=4.34, p=0.021). Of the Ranch Hands in the high dioxin category, 2.1 percent had low prealbumin levels versus 0.8 percent of the Comparisons. The Model 4 unadjusted and adjusted analyses were nonsignificant (Table 13-42(g,h): p>0.93 for each analysis).

13.2.2.3.34 Albumin (Continuous)

All unadjusted and adjusted Model 1 and 2 analyses were nonsignificant (Table 13-43(a–d): p>0.18 for each analysis).

Table 13-43. Analysis of Albumin (mg/dl) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean	Difference of Means (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***4,195.6***	***–5.6 (–34.9,23.8)***	***0.709***
	Comparison	***1,231***	***4,201.2***		
Officer	Ranch Hand	340	4,172.9	–31.8 (–78.3,14.8)	0.181
	Comparison	490	4,204.6		
Enlisted Flyer	Ranch Hand	150	4,190.0	30.1 (–42.4,102.5)	0.416
	Comparison	185	4,159.9		
Enlisted Groundcrew	Ranch Hand	369	4,218.8	7.0 (–37.3,51.2)	0.758
	Comparison	556	4,211.9		

Table 13-43. Analysis of Albumin (mg/dl) (Continuous) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adj. Mean	Difference of Adj. Means (95% C.I.)	p-Value
All	***Ranch Hand***	***854***	***4,180.8***	***–3.0 (–32.1,26.0)***	***0.837***
	Comparison	***1,229***	***4,183.8***		
Officer	Ranch Hand	340	4,163.1	–28.9 (–74.9,17.1)	0.218
	Comparison	489	4,192.1		
Enlisted Flyer	Ranch Hand	148	4,201.9	37.0 (–35.0,109.0)	0.314
	Comparison	184	4,164.9		
Enlisted Groundcrew	Ranch Hand	366	4,190.5	5.8 (–38.1,49.6)	0.797
	Comparison	556	4,184.7		

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Mean	Adj. Mean[a]	R^2	Slope (Std. Error)	p-Value
Low	158	4,170.0	4,164.4	0.023	13.830 (10.970)	0.208
Medium	159	4,163.0	4,162.4			
High	159	4,221.3	4,227.5			

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean	R^2	Adj. Slope (Std. Error)	p-Value
Low	158	4,148.8	0.054	–1.264 (12.791)	0.921
Medium	158	4,133.0			
High	157	4,169.0			

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,194	4,199.1	4,199.7		
Background RH	376	4,212.2	4,200.6	0.9 (–37.7,39.6)	0.962
Low RH	236	4,151.7	4,155.3	–44.5 (–90.8,1.8)	0.060
High RH	240	4,217.3	4,228.9	29.2 (–16.9,75.3)	0.215
Low plus High RH	476	4,184.8	4,192.4	–7.3 (–42.6,28.0)	0.685

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 13-43. Analysis of Albumin (mg/dl) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,193	4,183.0		
Background RH	374	4,187.9	5.0 (–34.0,43.9)	0.803
Low RH	235	4,154.2	–28.7 (–74.7,17.3)	0.221
High RH	238	4,200.2	17.2 (–30.0,64.4)	0.476
Low plus High RH	473	4,177.3	–5.6 (–41.0,29.8)	0.755

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean	R^2	Adjusted Slope (Std. Error)	p-Value
Low	283	4,227.5	<0.001	–2.471 (7.678)	0.748
Medium	285	4,153.4			
High	284	4,210.1			

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean	R^2	Adjusted Slope (Std. Error)	p-Value
Low	283	4,223.1	0.040	–11.121 (8.711)	0.202
Medium	283	4,157.9			
High	281	4,181.3			

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

The unadjusted Model 3 analysis showed a marginally significant difference between Ranch Hands in the low dioxin category and Comparisons (Table 13-43(e): difference of means=–44.5 mg/dl, p=0.060). No significant differences were noted in the adjusted Model 3 analysis of albumin (Table 13-43(f): p>0.22 for each contrast). In the Model 4 unadjusted and adjusted analyses of albumin, no significant associations with 1987 dioxin were found (Table 13-43(g,h): p>0.20 for each analysis).

13.2.2.3.35 Albumin (Discrete)

Because of a sparse number of low albumin values among the participants, some analyses were not possible. Table 13-44 contains the results of these analyses. Unadjusted chi-square tests of association in Model 3 revealed a significantly smaller percentage of Ranch Hands in the low and high dioxin categories combined with a low albumin level than Comparisons (Table 13-44(e): p=0.099). All other analyses in Models 1 through 4 were nonsignificant (Table 13-44(a–h): p≥0.17 for all other analyses).

Table 13-44. Analysis of Albumin (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Low	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***3 (0.3)***	***0.43 (0.12,1.56)***	***0.170***
	Comparison	***1,231***	***10 (0.8)***		
Officer	Ranch Hand	340	3 (0.9)	1.08 (0.24,4.86)	0.919
	Comparison	490	4 (0.8)		
Enlisted Flyer	Ranch Hand	150	0 (0.0)	--	0.999[a]
	Comparison	185	1 (0.5)		
Enlisted Groundcrew	Ranch Hand	369	0 (0.0)	--	0.171[a]
	Comparison	556	5 (0.9)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a low albumin level.

--: Results not presented because of the sparse number of participants with a low albumin level.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.45 (0.12,1.65)***	***0.200***
Officer	1.08 (0.24,4.91)	0.918
Enlisted Flyer	--	--
Enlisted Groundcrew	--	--

--: Results not presented because of the sparse number of participants with a low albumin level.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Low	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	158	0 (0.0)	--	--
Medium	159	0 (0.0)		
High	159	0 (0.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

--: Results not presented because of the sparse number of Ranch Hands with a low albumin level.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log$_2$ (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
--	--	--

[a] Relative risk for a twofold increase in initial dioxin.

--: Results not presented because of the sparse number of Ranch Hands with a low albumin level.

Table 13-44. Analysis of Albumin (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	**n**	**Number (%) Low**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,194	10 (0.8)		
Background RH	376	2 (0.5)	0.68 (0.15,3.14)	0.618
Low RH	236	0 (0.0)	--	0.325[c]
High RH	240	0 (0.0)	--	0.318[c]
Low plus High RH	476	0 (0.0)	--	0.099[c]

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] P-value determined using a chi-square test with continuity correction because of the sparse number of Ranch Hands with a low albumin level.
--: Results not presented because of the sparse number of Ranch Hands with a low albumin level.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Comparison	1,193		
Background RH	374	0.67 (0.14,3.20)	0.611
Low RH	235	--	--
High RH	238	--	--
Low plus High RH	473	--	--

[a] Relative risk and confidence interval relative to Comparisons.
--: Results not presented because of the sparse number of Ranch Hands with a low albumin level.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**	
1987 Dioxin	**n**	**Number (%) Low**	**Estimated Relative Risk (95% C.I.)[a]**	**p-Value**
Low	283	1 (0.4)	0.68 (0.24,1.96)	0.465
Medium	285	1 (0.4)		
High	284	0 (0.0)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 13-44. Analysis of Albumin (Discrete) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
847	0.52 (0.09,3.01)	0.442

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race, occupation, and industrial chemical exposure because of the sparse number of participants with a low albumin level.

13.2.2.3.36 α-1-Acid Glycoprotein (Continuous)

The Model 1 unadjusted and adjusted analyses of α-1-acid glycoprotein revealed no overall difference between Ranch Hands and Comparisons (Table 13-45(a,b): p>0.46 for each analysis). After stratifying by occupation, a significant difference between Ranch Hands and Comparisons was discovered among the enlisted groundcrew for both the unadjusted and adjusted analyses (Table 13-45(a,b): difference of means=2.61 mg/dl, p=0.044, for the unadjusted analysis; difference of adjusted means=2.76 mg/dl, p=0.030, for the adjusted analysis). The adjusted mean α-1-acid glycoprotein level among the Ranch Hand enlisted groundcrew was 86.86 mg/dl versus 84.10 mg/dl among the Comparison enlisted groundcrew.

The unadjusted Model 2 analysis was not significant (Table 13-45(c): p=0.992). After covariate adjustment, a marginally significant inverse relation between α-1-acid glycoprotein and initial dioxin was detected (Table 13-45(d): adjusted slope=–0.016, p=0.086). The adjusted mean α-1-acid glycoprotein levels in the low, medium, and high initial dioxin categories were 82.09 mg/dl, 83.12 mg/dl, and 79.32 mg/dl, respectively.

Table 13-45. Analysis of α-1-Acid Glycoprotein (mg/dl) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***859***	***84.65***	***0.50 --***	***0.550***
	Comparison	***1,231***	***84.15***		
Officer	Ranch Hand	340	80.89	–1.33 --	0.298
	Comparison	490	82.22		
Enlisted Flyer	Ranch Hand	150	85.49	–0.38 --	0.855
	Comparison	185	85.88		
Enlisted Groundcrew	Ranch Hand	369	87.92	2.61 --	0.044
	Comparison	556	85.31		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 13-45. Analysis of α-1-Acid Glycoprotein (mg/dl) (Continuous) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***854***	***83.11***	***0.60 --***	***0.464***
	Comparison	***1,229***	***82.51***		
Officer	Ranch Hand	340	78.64	−1.43 --	0.248
	Comparison	489	80.08		
Enlisted Flyer	Ranch Hand	148	83.83	0.15 --	0.942
	Comparison	184	83.68		
Enlisted Groundcrew	Ranch Hand	366	86.86	2.76 --	0.030
	Comparison	556	84.10		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	158	84.39	84.41	<0.001	0.000 (0.008)	0.992
Medium	159	87.88	87.88			
High	159	85.33	85.32			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of α-1-acid glycoprotein versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	158	82.09	0.046	−0.016 (0.009)	0.086
Medium	158	83.12			
High	157	79.32			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of α-1-acid glycoprotein versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 13-45. Analysis of α-1-Acid Glycoprotein (mg/dl) (Continuous) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,194	84.28	84.29		
Background RH	376	83.12	83.02	−1.27 --	0.256
Low RH	236	84.79	84.82	0.53 --	0.692
High RH	240	86.92	87.02	2.73 --	0.045
Low plus High RH	476	85.86	85.92	1.63 --	0.114

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,193	82.72		
Background RH	374	82.67	−0.05 --	0.961
Low RH	235	83.42	0.70 --	0.600
High RH	238	83.78	1.06 --	0.436
Low plus High RH	473	83.60	0.88 --	0.389

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	83.77	0.001	0.005 (0.005)	0.336
Medium	285	83.02			
High	284	87.18			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of α-1-acid glycoprotein versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 13-45. *Analysis of α-1-Acid Glycoprotein (mg/dl) (Continuous) (Continued)*

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	82.64	0.056	–0.012 (0.006)	0.049
Medium	283	80.92			
High	281	81.52			

[a] Transformed from natural logarithm scale.

[b] Slope and standard error based on natural logarithm of α-1-acid glycoprotein versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

In the Model 3 unadjusted analysis of α-1-acid glycoprotein, a significant difference between Ranch Hands in the high dioxin category and Comparisons was found (Table 13-45(e): difference of means=2.73 mg/dl, p=0.045). The adjusted analysis showed no significant contrasts between each of the dioxin categories and Comparisons (Table 13-45(f): p>0.38 for each contrast).

No significant association between α-1-acid glycoprotein and 1987 dioxin was revealed in the unadjusted Model 4 analysis (Table 13-45(g): p=0.336). After covariate adjustment, a significant inverse relation was found (Table 13-45(h): adjusted slope=–0.012, p=0.049). The mean α-1-acid glycoprotein levels in the low, medium, and high 1987 dioxin categories were 82.64 mg/dl, 80.92 mg/dl, and 81.52 mg/dl, respectively.

13.2.2.3.37 α-1-Acid Glycoprotein (Discrete)

The unadjusted analysis of α-1-acid glycoprotein in Model 1 did not show a significant group difference between Ranch Hands and Comparisons overall or after stratifying by occupation (Table 13-46(a): p>0.10 for each contrast). The adjusted analysis revealed a marginally significant difference between Ranch Hands and Comparisons among the enlisted groundcrew stratum (Table 13-46(b): Adj. RR=1.86, p=0.066). The percentage of Ranch Hand enlisted groundcrew with high α-1-acid glycoprotein levels was 5.4 versus 3.2 of Comparison enlisted groundcrew.

Table 13-46. Analysis of α-1-Acid Glycoprotein (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***37 (4.3)***	***1.34 (0.85,2.11)***	***0.209***
	Comparison	***1,231***	***40 (3.2)***		
Officer	Ranch Hand	340	8 (2.4)	0.76 (0.32,1.82)	0.542
	Comparison	490	15 (3.1)		
Enlisted Flyer	Ranch Hand	150	9 (6.0)	1.62 (0.59,4.47)	0.348
	Comparison	185	7 (3.8)		
Enlisted Groundcrew	Ranch Hand	369	20 (5.4)	1.71 (0.89,3.28)	0.105
	Comparison	556	18 (3.2)		

Table 13-46. Analysis of α-1-Acid Glycoprotein (Discrete) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1.39 (0.88,2.21)*	*0.163*
Officer	0.73 (0.31,1.76)	0.487
Enlisted Flyer	1.78 (0.64,4.95)	0.270
Enlisted Groundcrew	1.86 (0.96,3.60)	0.066

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	158	6 (3.8)	1.00 (0.72,1.38)	0.991
Medium	159	10 (6.3)		
High	159	7 (4.4)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
473	0.92 (0.63,1.35)	0.684

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,194	39 (3.3)		
Background RH	376	13 (3.5)	1.00 (0.52,1.90)	0.992
Low RH	236	11 (4.7)	1.47 (0.74,2.91)	0.272
High RH	240	12 (5.0)	1.65 (0.85,3.21)	0.141
Low plus High RH	476	23 (4.8)	1.56 (0.92,2.64)	0.101

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 13-46. Analysis of α-1-Acid Glycoprotein (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,193		
Background RH	374	1.12 (0.58,2.16)	0.745
Low RH	235	1.47 (0.73,2.94)	0.279
High RH	238	1.54 (0.77,3.08)	0.222
Low plus High RH	473	1.50 (0.88,2.58)	0.138

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	283	11 (3.9)	1.00 (0.80,1.25)	0.986
Medium	285	9 (3.2)		
High	284	16 (5.6)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
847	0.87 (0.68,1.11)	0.261

[a] Relative risk for a twofold increase in 1987 dioxin.

All unadjusted and adjusted analyses in Models 2 through 4 showed no significant relation between dioxin and dichotomized α-1-acid glycoprotein (Table 13-46(c–h): p>0.10 for each analysis).

13.2.2.3.38 α-1-Antitrypsin (Continuous)

Both the unadjusted and adjusted Model 1 analyses of α-1-antitrypsin revealed significant overall group differences (Table 13-47(a,b): difference of means=3.5 mg/dl, p=0.002; difference of adjusted means=3.6 mg/dl, p=0.001, respectively). The adjusted mean α-1-antitrypsin level was 146.7 mg/dl for all Ranch Hands and 143.1 mg/dl for all Comparisons. After stratifying by occupation, the unadjusted and adjusted analyses each showed a significant difference between Ranch Hands and Comparisons among the enlisted groundcrew (Table 13-47(a,b): difference of means=5.5 mg/dl, p=0.001, unadjusted; difference of adjusted means=5.9 mg/dl, p<0.001, adjusted). In addition, stratifying by occupation in the adjusted analysis revealed a marginally significant difference between Ranch Hands and Comparisons within the

enlisted flyer stratum (Table 13-47(b): difference of adjusted means=4.7 mg/dl, p=0.086). The adjusted mean α-1-antitrypsin levels for Ranch Hands and Comparisons in the enlisted flyer stratum were 150.5 mg/dl and 145.9 mg/dl, respectively. Within the enlisted groundcrew stratum, the adjusted mean α-1-antitrypsin levels were 151.5 mg/dl and 145.6 mg/dl for Ranch Hands and Comparisons, respectively.

Table 13-47. Analysis of α-1-Antitrypsin (mg/dl) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***859***	***150.0***	***3.5 --***	***0.002***
	Comparison	***1,231***	***146.5***		
Officer	Ranch Hand	340	143.9	0.9 --	0.609
	Comparison	490	143.0		
Enlisted Flyer	Ranch Hand	150	155.3	4.2 --	0.136
	Comparison	185	151.1		
Enlisted Groundcrew	Ranch Hand	369	153.5	5.5 --	0.001
	Comparison	556	148.0		

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***854***	***146.7***	***3.6 --***	***0.001***
	Comparison	***1,229***	***143.1***		
Officer	Ranch Hand	340	138.6	0.7 --	0.693
	Comparison	489	137.9		
Enlisted Flyer	Ranch Hand	148	150.5	4.7 --	0.086
	Comparison	184	145.9		
Enlisted Groundcrew	Ranch Hand	366	151.5	5.9 --	<0.001
	Comparison	556	145.6		

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

Table 13-47. Analysis of α-1-Antitrypsin (mg/dl) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	158	148.4	148.2	0.013	0.066 (0.036)	0.071
Medium	159	153.8	153.7			
High	159	151.8	152.1			

[a] Transformed from square root scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on square root of α-1-antitrypsin versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	158	145.0	0.101	0.023 (0.041)	0.582
Medium	158	148.8			
High	157	145.6			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of α-1-antitrypsin versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,194	146.8	146.8		
Background RH	376	148.0	147.9	1.1 --	0.470
Low RH	236	148.8	148.9	2.1 --	0.244
High RH	240	153.8	154.0	7.2 --	<0.001
Low plus High RH	476	151.3	151.4	4.6 --	0.001

[a] Transformed from square root scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[d] P-value is based on difference of means on square root scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 13-47. Analysis of α-1-Antitrypsin (mg/dl) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,193	143.8		
Background RH	374	147.2	3.4 --	0.024
Low RH	235	145.5	1.7 --	0.339
High RH	238	148.4	4.6 --	0.011
Low plus High RH	473	147.0	3.2 --	0.020

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	148.3	0.003	0.040 (0.025)	0.109
Medium	285	148.2			
High	284	153.1			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of α-1-antitrypsin versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	147.2	0.102	–0.047 (0.027)	0.089
Medium	283	145.2			
High	281	145.0			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of α-1-antitrypsin versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

The unadjusted Model 2 analysis revealed a marginally significant positive association between α-1-antitrypsin and initial dioxin (Table 13-47(c): slope=0.066, p=0.071). After adjusting for covariates, the relation became nonsignificant (Table 13-47(d): p=0.582).

The unadjusted Model 3 analysis revealed a marginally significant difference in mean α-1-antitrypsin levels between Ranch Hands in the high dioxin category and Comparisons, as well as between Ranch Hands in the low and high dioxin categories combined and Comparisons (Table 13-47(e): difference of means=7.2 mg/dl, p<0.001; difference of means=4.6 mg/dl, p=0.001, respectively).

Three significant contrasts were found in the adjusted Model 3 analysis of α-1-antitrypsin: Ranch Hands in the background dioxin category versus Comparisons (Table 13-47(f): difference of adjusted means=3.4 mg/dl, p=0.024), Ranch Hands in the high dioxin category versus Comparisons (difference of adjusted means=4.6 mg/dl, p=0.011), and Ranch Hands in the low and high dioxin categories combined versus Comparisons (difference of adjusted means=3.2 mg/dl, p=0.020). The adjusted mean α-1-antitrypsin levels for Ranch Hands in the background dioxin category, Ranch Hands in the high dioxin category, Ranch Hands in the low and high dioxin categories combined, and Comparisons were 147.2 mg/dl, 148.4 mg/dl, 147.0 mg/dl, and 143.8 mg/dl, respectively.

The unadjusted Model 4 analysis results were nonsignificant (Table 13-47(g): p=0.109). After adjusting for covariates, a marginally significant inverse relation between α-1-antitrypsin and 1987 dioxin was seen (Table 13-47(g): adjusted slope=–0.047, p=0.089). The adjusted mean α-1-antitrypsin levels in the low, medium, and high 1987 dioxin categories were 147.2 mg/dl, 145.2 mg/dl, and 145.0 mg/dl, respectively.

13.2.2.3.39 α-1-Antitrypsin (Discrete)

All unadjusted and adjusted results for Models 1 through 4 did not reveal a significant association between the percentage of individuals with low α-1-antitrypsin levels and dioxin or between the percentage of individuals with high α-1-antitrypsin levels and dioxin (Table 13-48(a–h): p>0.11 for all analyses).

Table 13-48. Analysis of α-1-Antitrypsin (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

			Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Occupational Category	Group	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)	p-Value	Est. Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*859*	*11 (1.3)*	*840 (97.8)*	*8 (0.9)*	*0.88 (0.41,1.87)*	*0.737*	*2.30 (0.75,7.06)*	*0.145*
	Comparison	*1,231*	*18 (1.5)*	*1,208 (98.1)*	*5 (0.4)*				
Officer	Ranch Hand	340	8 (2.4)	330 (97.1)	2 (0.6)	1.06 (0.42,2.65)	0.908	--	0.327[a]
	Comparison	490	11 (2.2)	479 (97.8)	0 (0.0)				
Enlisted Flyer	Ranch Hand	150	1 (0.7)	148 (98.7)	1 (0.7)	1.23 (0.08,19.83)	0.884	0.61 (0.07,5.25)	0.657
	Comparison	185	1 (0.5)	182 (98.4)	2 (1.1)				
Enlisted Groundcrew	Ranch Hand	369	2 (0.5)	362 (98.1)	5 (1.4)	0.50 (0.10,2.51)	0.403	2.52 (0.61,10.42)	0.202
	Comparison	556	6 (1.1)	547 (98.4)	3 (0.5)				

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with abnormal high α-1-antitrypsin levels.

--: Results not presented because of the sparse number of participants with abnormal high α-1-antitrypsin levels.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

	Abnormal Low vs. Normal		Abnormal High vs. Normal	
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Adj. Relative Risk (95% C.I.)	p-Value
All	*0.81 (0.37,1.78)*	*0.606*	*2.51 (0.80,7.90)*	*0.116*
Officer	1.10 (0.44,2.78)	0.834	--	--
Enlisted Flyer	--	--	0.73 (0.08,6.49)	0.778
Enlisted Groundcrew	0.47 (0.10,2.34)	0.358	2.69 (0.63,11.58)	0.183

--: Results not presented because of the sparse number of participants with abnormal α-1-antitrypsin levels.

Note: Results are not adjusted for race because of the sparse number of participants with abnormal α-1-antitrypsin levels.

Table 13-48. Analysis of α-1-Antitrypsin (Discrete) (Continued)

(c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category Summary Statistics					Analysis Results for Log_2 (Initial Dioxin)[a]			
		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Initial Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
Low	158	1 (0.6)	156 (98.7)	1 (0.6)	0.83 (0.37,1.90)	0.667	1.05 (0.39,2.80)	0.925
Medium	159	2 (1.3)	156 (98.1)	1 (0.6)				
High	159	1 (0.6)	157 (98.7)	1 (0.6)				

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)			
	Abnormal Low vs. Normal		Abnormal High vs. Normal	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
473	0.75 (0.30,1.84)	0.526	0.80 (0.21,3.00)	0.735

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race, occupation, current wine consumption, and degreasing chemical exposure because of the sparse number of participants with abnormal α-1-antitrypsin levels.

Table 13-48. Analysis of α-1-Antitrypsin (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[ab]	p-Value	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,194	17 (1.4)	1,172 (98.2)	5 (0.4)				
Background RH	376	7 (1.9)	364 (96.8)	5 (1.3)	1.14 (0.47,2.79)	0.772	2.48 (0.70,8.77)	0.158
Low RH	236	2 (0.8)	233 (98.7)	1 (0.4)	0.61 (0.14,2.67)	0.513	1.03 (0.11,9.33)	0.976
High RH	240	2 (0.8)	236 (98.3)	2 (0.8)	0.68 (0.16,2.98)	0.610	3.49 (0.64,19.06)	0.149
Low plus High RH	476	4 (0.8)	469 (98.5)	3 (0.6)	0.65 (0.22,1.93)	0.434	1.91 (0.42,8.72)	0.404

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

		Abnormal Low vs. Normal		Abnormal High vs. Normal	
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,193				
Background RH	374	0.78 (0.30,2.01)	0.602	2.76 (0.74,10.35)	0.131
Low RH	235	0.76 (0.17,3.35)	0.712	1.16 (0.13,10.62)	0.895
High RH	238	1.41 (0.28,7.06)	0.677	2.64 (0.43,16.23)	0.295
Low plus High RH	473	1.03 (0.32,3.31)	0.955	1.75 (0.36,8.53)	0.486

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.
Results are not adjusted for race because of the sparse number of participants with abnormal α-1-antitrypsin levels.

Table 13-48. Analysis of α-1-Antitrypsin (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS — 1987 DIOXIN — UNADJUSTED								
	1987 Dioxin Category Summary Statistics				Analysis Results for Log_2 (1987 Dioxin + 1)			
		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
1987 Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[a]	p-Value	Est. Relative Risk (95% C.I.)[a]	p-Value
Low	283	5 (1.8)	274 (96.8)	4 (1.4)	0.76 (0.49,1.19)	0.229	0.80 (0.48,1.33)	0.393
Medium	285	3 (1.1)	280 (98.2)	2 (0.7)				
High	284	3 (1.1)	279 (98.2)	2 (0.7)				

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9-19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS — 1987 DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (1987 Dioxin + 1)			
	Abnormal Low vs. Normal		Abnormal High vs. Normal	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
847	0.84 (0.52,1.37)	0.486	0.75 (0.44,1.29)	0.302

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race and occupation because of the sparse number of participants with abnormal α-1-antitrypsin levels.

13.2.2.3.40 α-2-Macroglobulin (Continuous)

All unadjusted and adjusted analyses of Models 1 through 4 showed no significant associations between dioxin and α-2-macroglobulin in its continuous form (Table 13-49(a–h): p>0.23 for each analysis).

Table 13-49. Analysis of α-2-Macroglobulin (mg/dl) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***859***	***170.6***	***–0.7 --***	***0.726***
	Comparison	***1,231***	***171.3***		
Officer	Ranch Hand	340	170.6	–0.4 --	0.901
	Comparison	490	171.0		
Enlisted Flyer	Ranch Hand	150	177.0	–0.4 --	0.935
	Comparison	185	177.4		
Enlisted Groundcrew	Ranch Hand	369	168.1	–1.5 --	0.608
	Comparison	556	169.6		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***854***	***161.9***	***–0.9 --***	***0.610***
	Comparison	***1,229***	***162.8***		
Officer	Ranch Hand	340	154.5	–1.2 --	0.643
	Comparison	489	155.7		
Enlisted Flyer	Ranch Hand	148	163.8	–1.9 --	0.664
	Comparison	184	165.7		
Enlisted Groundcrew	Ranch Hand	366	167.4	–0.2 --	0.951
	Comparison	556	167.6		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 13-49. Analysis of α-2-Macroglobulin (mg/dl) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	158	168.1	168.1	<0.001	–0.004 (0.009)	0.698
Medium	159	175.3	175.3			
High	159	167.4	167.4			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of α-2-macroglobulin versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	158	154.2	0.135	0.009 (0.010)	0.368
Medium	158	163.5			
High	157	161.3			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of α-2-macroglobulin versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,194	171.2	171.2		
Background RH	376	170.2	170.2	–1.0 --	0.706
Low RH	236	170.2	170.2	–1.0 --	0.747
High RH	240	170.2	170.2	–1.0 --	0.741
Low plus High RH	476	170.2	170.2	–1.0 --	0.669

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 13-49. Analysis of α-2-Macroglobulin (mg/dl) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,193	163.2		
Background RH	374	162.2	–1.0 --	0.683
Low RH	235	159.9	–3.3 --	0.232
High RH	238	163.3	0.1 --	0.959
Low plus High RH	473	161.6	–1.6 --	0.461

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	169.9	<0.001	–0.004 (0.006)	0.522
Medium	285	170.6			
High	284	170.2			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of α-2-macroglobulin versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	162.9	0.131	–0.005 (0.006)	0.390
Medium	283	161.1			
High	281	162.8			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of α-2-macroglobulin versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

13.2.2.3.41 α-2-Macroglobulin (Discrete)

The unadjusted and adjusted Model 1 analyses of α-2-macroglobulin were nonsignificant (Table 13-50(a,b): p>0.15 for each analysis). The unadjusted Model 2 analysis was not significant (Table 13-50(c): p=0.254), but the adjusted analysis was marginally significant (Table 13-50(d): Adj. RR=1.48, p=0.072).

The unadjusted Model 3 analysis revealed a marginally significant difference in high α-2-macroglobulin levels between Ranch Hands in the background dioxin category and Comparisons (Table 13-50(e): Est. RR=0.46, p=0.080). The percentage of Ranch Hands in the background category with high α-2-macroglobulin levels was 1.6 versus 3.8 for Comparisons. The same contrast was marginally significant in the adjusted Model 3 analysis (Table 13-50(f): Adj. RR=0.45, p=0.079).

Table 13-50. Analysis of α-2-Macroglobulin (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***24 (2.8)***	***0.72 (0.44,1.19)***	***0.199***
	Comparison	***1,231***	***47 (3.8)***		
Officer	Ranch Hand	340	8 (2.4)	0.63 (0.27,1.47)	0.287
	Comparison	490	18 (3.7)		
Enlisted Flyer	Ranch Hand	150	5 (3.3)	0.55 (0.19,1.61)	0.271
	Comparison	185	11 (5.9)		
Enlisted Groundcrew	Ranch Hand	369	11 (3.0)	0.92 (0.43,1.97)	0.827
	Comparison	556	18 (3.2)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.70 (0.42,1.16)***	***0.157***
Officer	0.59 (0.25,1.40)	0.234
Enlisted Flyer	0.46 (0.15,1.39)	0.169
Enlisted Groundcrew	1.01 (0.46,2.19)	0.988

Note: Results are not adjusted for race because of the sparse number of participants with high α-2-macroglobulin levels.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	158	2 (1.3)	1.22 (0.87,1.71)	0.254
Medium	159	10 (6.3)		
High	159	5 (3.1)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 13-50. Analysis of α-2-Macroglobulin (Discrete) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
473	1.48 (0.96,2.27)	0.072

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race because of the sparse number of Ranch Hands with high α-2-macroglobulin levels.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,194	45 (3.8)		
Background RH	376	6 (1.6)	0.46 (0.19,1.10)	0.080
Low RH	236	7 (3.0)	0.75 (0.33,1.69)	0.492
High RH	240	10 (4.2)	1.00 (0.49,2.03)	0.999
Low plus High RH	476	17 (3.6)	0.87 (0.49,1.55)	0.632

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,193		
Background RH	374	0.45 (0.19,1.10)	0.079
Low RH	235	0.61 (0.27,1.40)	0.246
High RH	238	1.09 (0.51,2.31)	0.823
Low plus High RH	473	0.82 (0.45,1.49)	0.511

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for race because of the sparse number of participants with high α-2-macroglobulin levels.

Table 13-50. Analysis of α-2-Macroglobulin (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	283	3 (1.1)	1.37 (1.06,1.77)	0.020
Medium	285	8 (2.8)		
High	284	12 (4.2)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
847	1.50 (1.08,2.08)	0.014

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race because of the sparse number of participants with high α-2-macroglobulin levels.

Both the unadjusted and adjusted Model 4 analyses revealed significant associations between α-2-macroglobulin and 1987 dioxin (Table 13-50(g,h): Est. RR=1.37, p=0.020; Adj. RR=1.50, p=0.014, respectively). The percentages of participants with high α-2-macroglobulin values in the low, medium, and high 1987 dioxin categories were 1.1, 2.8, and 4.2, respectively.

13.2.2.3.42 Apolipoprotein B (mg/dl) (Continuous)

The Model 1 analysis of apolipoprotein B did not show a significant overall difference between Ranch Hands and Comparisons in either the unadjusted or adjusted analyses (Table 13-51(a,b): p>0.27 for each analysis). After stratifying by occupation, a significant difference between Ranch Hands and Comparisons was discovered among the officers in both the unadjusted and adjusted analyses (Table 13-51(a,b): difference of means=–3.3 mg/dl, p=0.053, for the unadjusted analysis; difference of adjusted means=–3.3 mg/dl, p=0.048, for the adjusted analysis). The adjusted mean apolipoprotein B level among the Ranch Hand officers was 105.9 mg/dl versus 109.2 mg/dl among the Comparison officers.

Table 13-51. Analysis of Apolipoprotein B (mg/dl) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***859***	***110.5***	***–1.1 --***	***0.320***
	Comparison	***1,231***	***111.5***		
Officer	Ranch Hand	340	106.4	–3.3 --	0.053
	Comparison	490	109.6		
Enlisted Flyer	Ranch Hand	150	113.2	–2.0 --	0.463
	Comparison	185	115.2		
Enlisted Groundcrew	Ranch Hand	369	113.1	1.2 --	0.479
	Comparison	556	112.0		

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***854***	***110.6***	***–1.2 --***	***0.275***
	Comparison	***1,229***	***111.8***		
Officer	Ranch Hand	340	105.9	–3.3 --	0.048
	Comparison	489	109.2		
Enlisted Flyer	Ranch Hand	148	112.9	–2.2 --	0.413
	Comparison	184	115.1		
Enlisted Groundcrew	Ranch Hand	366	112.6	1.2 --	0.457
	Comparison	556	111.4		

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	158	107.1	107.0	0.014	0.107 (0.041)	0.009
Medium	159	113.9	113.9			
High	159	114.5	114.6			

[a] Transformed from square root scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on square root of apolipoprotein B versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 13-51. Analysis of Apolipoprotein B (mg/dl) (Continuous) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	158	108.5	0.033	0.061 (0.048)	0.209
Medium	158	113.8			
High	157	113.2			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of apolipoprotein B versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,194	111.5	111.5		
Background RH	376	108.8	108.8	–2.7 --	0.057
Low RH	236	108.9	108.9	–2.6 --	0.131
High RH	240	114.7	114.6	3.1 --	0.073
Low plus High RH	476	111.8	111.8	0.3 --	0.843

[a] Transformed from square root scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[d] P-value is based on difference of means on square root scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,193	112.0		
Background RH	374	110.0	–2.0 --	0.170
Low RH	235	109.5	–2.5 --	0.154
High RH	238	113.6	1.6 --	0.358
Low plus High RH	473	111.6	–0.4 --	0.761

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 13-51. Analysis of Apolipoprotein B (mg/dl) (Continuous) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	109.2	0.011	0.083 (0.027)	0.002
Medium	285	108.0			
High	284	114.2			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of apolipoprotein B versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	111.0	0.023	0.046 (0.031)	0.142
Medium	283	109.0			
High	281	112.9			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of apolipoprotein B versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

The unadjusted Model 2 analysis revealed a significant relation between initial dioxin and apolipoprotein B (Table 13-51(c): slope=0.107, p=0.009). The adjusted analysis results were not significant (Table 13-51(d): p=0.209).

The unadjusted Model 3 analysis revealed two marginally significant contrasts: Ranch Hands in the background dioxin category versus Comparisons and Ranch Hands in the high dioxin category versus Comparisons (Table 13-51(e): difference of means=–2.7 mg/dl, p=0.057; difference of means=3.1 mg/dl, p=0.073, respectively). After adjusting for covariates, no contrasts were significant (Table 13-51(f): p>0.15 for each contrast).

The Model 4 unadjusted analysis of apolipoprotein B revealed a significant association with 1987 dioxin (Table 13-51(g): slope=0.083, p=0.002). The adjusted analysis was nonsignificant (Table 13-51(h): p=0.142).

The reference range between 1992 and 1997 decreased according to the manufacturer's recommendation. Consequently, the mean levels shown in Table 13-51 are less than the 1992 mean levels.

13.2.2.3.43 Apolipoprotein B (Discrete)

Both the unadjusted and adjusted Model 1 analyses of apolipoprotein B in its dichotomous form revealed marginally significant overall group differences (Table 13-52(a,b): Est. RR=0.86, p=0.087; Adj. RR=0.85, p=0.073, respectively). After stratifying by occupation, unadjusted and adjusted analyses revealed group differences within the enlisted flyer stratum (Table 13-52(a,b): Est. RR=0.55, p=0.007; Adj. RR=0.53, p=0.005, respectively). The percentage of participants in the Ranch Hand group with high

apolipoprotein B values was 49.2 versus 53.0 for Comparisons. Within the enlisted flyer stratum, 48.0 percent of the Ranch Hands had high apolipoprotein B values versus 62.7 percent of the Comparisons. The unadjusted Model 2 analysis revealed a marginally significant association between apolipoprotein B and initial dioxin (Table 13-52(c): Est. RR=1.14, p=0.059). The adjusted analysis showed no significant results (Table 13-52(d): p=0.456).

Table 13-52. Analysis of Apolipoprotein B (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***423 (49.2)***	***0.86 (0.72,1.02)***	***0.087***
	Comparison	***1,231***	***653 (53.0)***		
Officer	Ranch Hand	340	149 (43.8)	0.80 (0.61,1.06)	0.114
	Comparison	490	242 (49.4)		
Enlisted Flyer	Ranch Hand	150	72 (48.0)	0.55 (0.35,0.85)	0.007
	Comparison	185	116 (62.7)		
Enlisted Groundcrew	Ranch Hand	369	202 (54.7)	1.07 (0.82,1.39)	0.615
	Comparison	556	295 (53.1)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.85 (0.71,1.02)***	***0.073***
Officer	0.80 (0.61,1.06)	0.115
Enlisted Flyer	0.53 (0.34,0.82)	0.005
Enlisted Groundcrew	1.07 (0.82,1.40)	0.603

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	158	73 (46.2)	1.14 (0.99,1.31)	0.059
Medium	159	84 (52.8)		
High	159	88 (55.3)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
473	1.06 (0.90,1.25)	0.456

[a] Relative risk for a twofold increase in initial dioxin.

Table 13-52. Analysis of Apolipoprotein B (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,194	636 (53.3)		
Background RH	376	174 (46.3)	0.75 (0.60,0.95)	0.017
Low RH	236	113 (47.9)	0.81 (0.61,1.07)	0.132
High RH	240	132 (55.0)	1.08 (0.81,1.42)	0.606
Low plus High RH	476	245 (51.5)	0.93 (0.75,1.16)	0.524

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,193		
Background RH	374	0.79 (0.62,1.00)	0.050
Low RH	235	0.82 (0.62,1.09)	0.164
High RH	238	0.97 (0.73,1.30)	0.849
Low plus High RH	473	0.89 (0.72,1.11)	0.305

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	283	135 (47.7)	1.12 (1.02,1.23)	0.017
Medium	285	130 (45.6)		
High	284	154 (54.2)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 13-52. Analysis of Apolipoprotein B (Discrete) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
847	1.07 (0.96,1.18)	0.242

[a] Relative risk for a twofold increase in 1987 dioxin.

Model 3 revealed significant relations between Ranch Hands in the background dioxin category and Comparisons for both the unadjusted and adjusted analyses (Table 13-52(e,f): Est. RR=0.75, p=0.017; Adj. RR=0.79, p=0.050, respectively). The percentage of high apolipoprotein B values among the Ranch Hands in the background dioxin category was 46.3 versus 53.3 for Comparisons.

The unadjusted Model 4 analysis of apolipoprotein B showed a significant association with 1987 dioxin (Table 13-52(g): Est. RR=1.12, p=0.017). After adjusting for covariates, the relation became nonsignificant (Table 13-52(h): p=0.242).

The reference range between 1992 and 1997 decreased according to the manufacturer's recommendation. The change may explain partially the decrease in the percentage of participants with high apolipoprotein B levels between 1992 and 1997.

13.2.2.3.44 C3 Complement (mg/dl) (Continuous)

The unadjusted and adjusted Model 1 analyses of C3 complement in its continuous form revealed no significant group differences (Table 13-53(a,b): p>0.50 for each analysis).

Table 13-53. Analysis of C3 Complement (mg/dl) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***859***	***118.9***	***0.4 --***	***0.640***
	Comparison	***1,231***	***118.5***		
Officer	Ranch Hand	340	114.9	0.3 --	0.814
	Comparison	490	114.6		
Enlisted Flyer	Ranch Hand	150	120.3	–0.4 --	0.862
	Comparison	185	120.7		
Enlisted Groundcrew	Ranch Hand	369	122.1	0.8 --	0.537
	Comparison	556	121.3		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 13-53. Analysis of C3 Complement (mg/dl) (Continuous) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***854***	***120.2***	***0.2 --***	***0.837***
	Comparison	***1,229***	***120.0***		
Officer	Ranch Hand	340	116.5	0.4 --	0.765
	Comparison	489	116.1		
Enlisted Flyer	Ranch Hand	148	120.8	−1.4 --	0.505
	Comparison	184	122.2		
Enlisted Groundcrew	Ranch Hand	366	122.8	0.6 --	0.668
	Comparison	556	122.3		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	158	118.3	118.8	0.071	0.012 (0.005)	0.023
Medium	159	123.6	123.7			
High	159	124.0	123.4			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of C3 complement versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	158	119.1	0.083	0.009 (0.006)	0.145
Medium	158	123.9			
High	157	122.7			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of C3 complement versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 13-53. Analysis of C3 Complement (mg/dl) (Continuous) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,194	118.5	118.5		
Background RH	376	115.2	116.7	–1.8 --	0.107
Low RH	236	120.0	119.5	1.0 --	0.399
High RH	240	123.9	122.3	3.8 --	0.003
Low plus High RH	476	122.0	120.9	2.4 --	0.013

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,193	120.1		
Background RH	374	119.5	–0.6 --	0.594
Low RH	235	121.0	0.9 --	0.518
High RH	238	121.8	1.7 --	0.217
Low plus High RH	473	121.4	1.3 --	0.213

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	115.1	0.040	0.021 (0.004)	<0.001
Medium	285	117.8			
High	284	124.1			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of C3 complement versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 13-53. Analysis of C3 Complement (mg/dl) (Continuous) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	117.6	0.067	0.017 (0.004)	<0.001
Medium	283	119.6			
High	281	124.6			

[a] Transformed from natural logarithm scale.

[b] Slope and standard error based on natural logarithm of C3 complement versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

A significant relation was found between initial dioxin and C3 complement in the unadjusted Model 2 analysis (Table 13-53(c): slope=0.012, p=0.023). The adjusted analysis was nonsignificant (Table 13-53(d): p=0.145).

The unadjusted Model 3 analysis revealed a significant difference in mean C3 complement levels between Ranch Hands in the high dioxin category and Comparisons, as well as between Ranch Hands in the low and high dioxin categories combined and Comparisons (Table 13-53(e): difference of means=3.8 mg/dl, p=0.003; difference of means=2.4 mg/dl, p=0.013, respectively). The adjusted analysis showed no significant differences between any of the Ranch Hand categories and Comparisons (Table 13-53(f): p>0.21 for each contrast).

Both the unadjusted and adjusted Model 4 analyses revealed significant associations between C3 complement and 1987 dioxin (Table 13-53(g,h): slope=0.021, p<0.001; adjusted slope=0.017, p<0.001, respectively). The adjusted mean C3 complement levels in the low, medium, and high 1987 dioxin categories were 117.6 mg/dl, 119.6 mg/dl, 124.6 mg/dl, respectively.

13.2.2.3.45 C3 Complement (Discrete)

The unadjusted and adjusted Model 1 analyses showed no significant difference in the percentage of low C3 complement values between Ranch Hands and Comparisons (Table 13-54(a,b): p>0.19 for each analysis).

Table 13-54. Analysis of C3 Complement (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Low	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***15 (1.7)***	***0.76 (0.41,1.44)***	***0.398***
	Comparison	***1,231***	***28 (2.3)***		
Officer	Ranch Hand	340	6 (1.8)	0.61 (0.23,1.61)	0.317
	Comparison	490	14 (2.9)		
Enlisted Flyer	Ranch Hand	150	1 (0.7)	0.24 (0.03,2.09)	0.197
	Comparison	185	5 (2.7)		
Enlisted Groundcrew	Ranch Hand	369	8 (2.2)	1.35 (0.51,3.52)	0.544
	Comparison	556	9 (1.6)		

Table 13-54. Analysis of C3 Complement (Discrete) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.79 (0.42,1.50)***	***0.474***
Officer	0.62 (0.23,1.63)	0.333
Enlisted Flyer	0.27 (0.03,2.33)	0.233
Enlisted Groundcrew	1.41 (0.54,3.71)	0.487

Note: Results are not adjusted for race because of the sparse number of participants with low C3 complement levels.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Low	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	158	1 (0.6)	1.06 (0.45,2.49)	0.898
Medium	159	1 (0.6)		
High	159	1 (0.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
473	1.01 (0.39,2.62)	0.977

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race and occupation because of the sparse number of Ranch Hands with low C3 complement levels.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Low	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,194	26 (2.2)		
Background RH	376	12 (3.2)	1.28 (0.63,2.57)	0.495
Low RH	236	1 (0.4)	0.20 (0.03,1.46)	0.111
High RH	240	2 (0.8)	0.44 (0.10,1.86)	0.261
Low plus High RH	476	3 (0.6)	0.29 (0.08,1.04)	0.057

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 13-54. Analysis of C3 Complement (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,193		
Background RH	374	1.25 (0.61,2.57)	0.536
Low RH	235	0.21 (0.03,1.57)	0.128
High RH	238	0.49 (0.11,2.17)	0.351
Low plus High RH	473	0.32 (0.09,1.16)	0.083

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for race because of the sparse number of participants with low C3 complement levels.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Low	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	283	10 (3.5)	0.61 (0.41,0.91)	0.011
Medium	285	3 (1.1)		
High	284	2 (0.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
847	0.57 (0.39,0.84)	0.004

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race because of the sparse number of Ranch Hands with low C3 complement levels.

The Model 2 unadjusted and adjusted analyses results were nonsignificant (Table 13-54(c,d): p>0.89 for each analysis). Both the unadjusted and adjusted Model 3 analyses revealed marginally significant differences between Ranch Hands in the low and high dioxin categories combined and Comparisons (Table 13-54(e,f): Est. RR=0.29, p=0.057; Adj. RR=0.32, p=0.083, respectively). The percentage of low C3 complement values for Ranch Hands in the low and high dioxin categories combined was 0.6 versus 2.2 in the Comparison category.

The Model 4 unadjusted and adjusted analyses each revealed a significant association between C3 complement and 1987 dioxin (Table 13-54(g,h): Est. RR=0.61, p=0.011; Adj. RR=0.57, p=0.004,

respectively). The percentages of low C3 complement values in the low, medium, and high 1987 dioxin categories were 3.5, 1.1, and 0.7, respectively.

13.2.2.3.46 C4 Complement (Continuous)

The Model 1 unadjusted analysis of C4 complement showed no overall group differences (Table 13-55(a,b): p>0.33 for each analysis). Stratifying by occupation revealed a significant difference between Ranch Hand and Comparison officers, as well as enlisted flyers (Table 13-55(a): difference of means=–0.81 mg/dl, p=0.024, for the officer stratum; difference of means=1.02 mg/dl, p=0.076, for the enlisted flyer stratum). After adjusting for covariates, a significant difference between Ranch Hands and Comparisons was noted only among the officer stratum (Table 13-55(b): difference of adjusted means=–0.90 mg/dl, p=0.017). The adjusted mean C4 complement value for Ranch Hand officers was 26.02 mg/dl versus 26.91 mg/dl for Comparison officers.

Table 13-55. Analysis of C4 Complement (mg/dl) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***859***	***25.71***	***–0.20 --***	***0.395***
	Comparison	***1,231***	***25.91***		
Officer	Ranch Hand	340	24.73	–0.81 --	0.024
	Comparison	490	25.54		
Enlisted Flyer	Ranch Hand	150	26.52	1.02 --	0.076
	Comparison	185	25.50		
Enlisted Groundcrew	Ranch Hand	369	26.31	–0.06 --	0.862
	Comparison	556	26.38		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***854***	***26.98***	***–0.23 --***	***0.333***
	Comparison	***1,229***	***27.21***		
Officer	Ranch Hand	340	26.02	–0.90 --	0.017
	Comparison	489	26.91		
Enlisted Flyer	Ranch Hand	148	27.74	0.98 --	0.104
	Comparison	184	26.77		
Enlisted Groundcrew	Ranch Hand	366	27.61	–0.06 --	0.876
	Comparison	556	27.67		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 13-55. Analysis of C4 Complement (mg/dl) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	158	25.70	25.72	0.002	–0.003 (0.007)	0.701
Medium	159	26.43	26.43			
High	159	26.07	26.05			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of C4 complement versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	158	26.58	0.019	–0.004 (0.008)	0.638
Medium	158	27.31			
High	157	27.01			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of C4 complement versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,194	25.91	25.90		
Background RH	376	25.26	25.41	–0.49 --	0.109
Low RH	236	26.07	26.03	0.13 --	0.733
High RH	240	26.06	25.91	0.01 --	0.986
Low plus High RH	476	26.06	25.97	0.07 --	0.816

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 13-55. Analysis of C4 Complement (mg/dl) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,193	27.24		
Background RH	374	26.93	–0.31 --	0.336
Low RH	235	27.27	0.03 --	0.942
High RH	238	26.97	–0.27 --	0.494
Low plus High RH	473	27.12	–0.12 --	0.680

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	25.10	0.004	0.009 (0.005)	0.070
Medium	285	25.85			
High	284	26.19			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of C4 complement versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	26.73	0.044	0.001 (0.005)	0.849
Medium	283	27.16			
High	281	27.02			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of C4 complement versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

The unadjusted and adjusted analyses for Models 2 and 3 showed no significant relation between dioxin and C4 complement (Table 13-55(c–f): p>0.10 for each analysis). A marginally significant association between 1987 dioxin and C4 complement was revealed in the unadjusted Model 4 analysis (Table 13-55(g): slope=0.009, p=0.070). After covariate adjustment, the adjusted analysis results became nonsignificant (Table 13-55(h): p=0.849).

13.2.2.3.47 C4 Complement (Discrete)

Because of a sparse number of low C4 complement values among the participants, some analyses were not possible. Table 13-56 contains the results of these analyses.

Table 13-56. Analysis of C4 Complement (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Low	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***2 (0.2)***	***1.43 (0.20,10.20)***	***0.719***
	Comparison	***1,231***	***2 (0.2)***		
Officer	Ranch Hand	340	2 (0.6)	2.89 (0.26,32.04)	0.386
	Comparison	490	1 (0.2)		
Enlisted Flyer	Ranch Hand	150	0 (0.0)	--	0.999[a]
	Comparison	185	1 (0.5)		
Enlisted Groundcrew	Ranch Hand	369	0 (0.0)	--	--
	Comparison	556	0 (0.0)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a low C4 complement level.
--: Results not presented because of the sparse number of participants with a low C4 complement level.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.46 (0.20,10.59)***	***0.707***
Officer	2.85 (0.26,31.68)	0.394
Enlisted Flyer	--	--
Enlisted Groundcrew	--	--

--: Results not presented because of the sparse number of participants with a low C4 complement level.

Note: Results for analysis across all occupational categories are not adjusted for race, occupation, and degreasing chemical exposure because of the sparse number of participants with a low C4 complement level; results for individual occupational categories are not adjusted for race and degreasing chemical exposure because of the sparse number of participants with a low C4 complement level.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Low	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	158	0 (0.0)	--	--
Medium	159	0 (0.0)		
High	159	0 (0.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.
--: Results not presented because of the sparse number of Ranch Hands with a low C4 complement level.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 13-56. Analysis of C4 Complement (Discrete) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)	p-Value
--	--	--

--: Results not presented because of the sparse number of Ranch Hands with a low C4 complement level.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Low	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,194	2 (0.2)		
Background RH	376	2 (0.5)	3.46 (0.47,25.38)	0.222
Low RH	236	0 (0.0)	--	0.999[c]
High RH	240	0 (0.0)	--	0.999[c]
Low plus High RH	476	0 (0.0)	--	0.913[c]

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a low C4 complement level.
--: Results not presented because of the sparse number of Ranch Hands with a low C4 complement level.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,193		
Background RH	374	2.99 (0.40,22.39)	0.286
Low RH	235	--	--
High RH	238	--	--
Low plus High RH	473	--	--

[a] Relative risk and confidence interval relative to Comparisons.
--: Results not presented because of the sparse number of Ranch Hands with a low C4 complement level.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for race, occupation, and degreasing chemical exposure because of the sparse number of participants with a low C4 complement level.

Table 13-56. Analysis of C4 Complement (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Low	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	283	2 (0.7)	0.32 (0.12,0.90)	0.033
Medium	285	0 (0.0)		
High	284	0 (0.0)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
847	0.26 (0.08,0.86)	0.024

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race, occupation, industrial chemical exposure, and degreasing chemical exposure because of the sparse number of Ranch Hands with a low C4 complement level.

Unadjusted and adjusted results for Models 1 through 3 revealed no significant associations between C4 complement in its dichotomous form and dioxin (Table 13-56(a–f): p>0.22 for each contrast). The unadjusted and adjusted Model 4 analyses revealed a significant relation between C4 complement and 1987 dioxin (Table 13-56(g,h): Est. RR=0.32, p=0.033; Adj. RR=0.26, p=0.024, respectively).

13.2.2.3.48 Haptoglobin (Continuous)

The unadjusted and adjusted Model 1 analyses of haptoglobin each revealed a significant overall group difference (Table 13-57(a,b): difference of means=8.7 mg/dl, p=0.002, for the unadjusted analysis; difference of means=8.0 mg/dl, p=0.003, for the adjusted analysis). The adjusted mean haptoglobin values for the Ranch Hands were 128.5 mg/dl versus 120.5 mg/dl for the Comparisons. After stratifying by occupation, both the unadjusted and adjusted analyses showed a significant difference in mean haptoglobin levels between Ranch Hands and Comparisons in the enlisted groundcrew stratum (Table 13-57(a,b): difference of means=10.2 mg/dl, p=0.016, for the unadjusted analysis; difference of adjusted means=9.9 mg/dl, p=0.016, for the adjusted analysis). The adjusted mean haptoglobin level among Ranch Hand enlisted groundcrew was 137.4 mg/dl versus 127.4 mg/dl among Comparison enlisted groundcrew.

Table 13-57. Analysis of Haptoglobin (mg/dl) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***859***	***135.2***	***8.7 --***	***0.002***
	Comparison	***1,231***	***126.5***		
Officer	Ranch Hand	340	122.4	6.1 --	0.140
	Comparison	490	116.3		
Enlisted Flyer	Ranch Hand	150	147.8	10.4 --	0.141
	Comparison	185	137.4		
Enlisted Groundcrew	Ranch Hand	369	142.5	10.2 --	0.016
	Comparison	556	132.3		

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***854***	***128.5***	***8.0 --***	***0.003***
	Comparison	***1,229***	***120.5***		
Officer	Ranch Hand	340	112.2	5.4 --	0.172
	Comparison	489	106.8		
Enlisted Flyer	Ranch Hand	148	137.3	9.5 --	0.160
	Comparison	184	127.8		
Enlisted Groundcrew	Ranch Hand	366	137.4	9.9 --	0.016
	Comparison	556	127.4		

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	158	130.2	130.3	0.002	0.084 (0.097)	0.387
Medium	159	144.4	144.5			
High	159	140.0	139.9			

[a] Transformed from square root scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on square root of haptoglobin versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 13-57. Analysis of Haptoglobin (mg/dl) (Continuous) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	158	118.8	0.066	–0.087 (0.111)	0.433
Medium	158	124.6			
High	157	116.4			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of haptoglobin versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,194	126.7	126.7		
Background RH	376	131.3	131.4	4.7 --	0.210
Low RH	236	134.6	134.5	7.8 --	0.078
High RH	240	141.8	141.7	15.0 --	0.001
Low plus High RH	476	138.2	138.1	11.4 --	0.001

[a] Transformed from square root scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[d] P-value is based on difference of means on square root scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,193	120.9		
Background RH	374	129.8	8.9 --	0.014
Low RH	235	127.5	6.6 --	0.118
High RH	238	128.0	7.1 --	0.105
Low plus High RH	473	127.7	6.8 --	0.036

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 13-57. Analysis of Haptoglobin (mg/dl) (Continuous) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	130.4	0.002	0.074 (0.065)	0.254
Medium	285	132.6			
High	284	142.5			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of haptoglobin versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	127.4	0.055	–0.116 (0.073)	0.114
Medium	283	125.1			
High	281	124.4			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of haptoglobin versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

The unadjusted and adjusted Model 2 analyses showed no significant relation between initial dioxin and haptoglobin (Table 13-57(c,d): p>0.38 for each analysis). Three significant contrasts were found in the unadjusted Model 3 analysis of haptoglobin: Ranch Hands in the low dioxin category versus Comparisons (Table 13-57(e): difference of means=7.8 mg/dl, p=0.078), Ranch Hands in the high dioxin category versus Comparisons (Table 13-57(e): difference of means=15.0 mg/dl, p=0.001), and Ranch Hands in the low and high dioxin categories combined versus Comparisons (Table 13-57(e): difference of means=11.4 mg/dl, p=0.001).

After adjusting for covariates, two contrasts were found to be significant in the Model 3 analysis: Ranch Hands in the background dioxin category versus Comparisons and Ranch Hands in the low and high dioxin categories combined versus Comparisons (Table 13-57(f): difference of adjusted means=8.9 mg/dl, p=0.014; difference of adjusted means=6.8 mg/dl, p=0.036, respectively). The adjusted mean haptoglobin levels for Ranch Hands in the background dioxin category, Ranch Hands in the low and high dioxin categories combined, and Comparisons were 129.8 mg/dl, 127.7 mg/dl, and 120.9 mg/dl respectively. No significant relation was determined between 1987 dioxin and haptoglobin in either the unadjusted or adjusted Model 4 analysis (Table 13-57(g,h): p>0.11 for each analysis).

13.2.2.3.49 Haptoglobin (Discrete)

A significant overall group difference was revealed in both the unadjusted and adjusted Model 1 analyses of haptoglobin in its discrete form (Table 13-58(a,b): Est. RR=1.26, p=0.017; Adj. RR=1.26, p=0.020, respectively). The percentage of Ranch Hands with high haptoglobin levels was 32.7 versus 27.9 for Comparisons. After stratifying by occupation, both the unadjusted and adjusted analyses revealed a marginally significant difference between Ranch Hands and Comparisons among the enlisted groundcrew

(Table 13-58(a,b): Est. RR=1.30, p=0.063; Adj. RR=1.31, p=0.061, respectively). The percentage of high haptoglobin levels among the Ranch Hand enlisted groundcrew was 37.4 versus 31.5 among the Comparison enlisted groundcrew.

Table 13-58. Analysis of Haptoglobin (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***281 (32.7)***	***1.26 (1.04,1.52)***	***0.017***
	Comparison	***1,231***	***343 (27.9)***		
Officer	Ranch Hand	340	84 (24.7)	1.19 (0.86,1.65)	0.300
	Comparison	490	106 (21.6)		
Enlisted Flyer	Ranch Hand	150	59 (39.3)	1.29 (0.82,2.01)	0.271
	Comparison	185	62 (33.5)		
Enlisted Groundcrew	Ranch Hand	369	138 (37.4)	1.30 (0.99,1.72)	0.063
	Comparison	556	175 (31.5)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.26 (1.04,1.52)***	***0.020***
Officer	1.18 (0.85,1.64)	0.316
Enlisted Flyer	1.27 (0.81,2.01)	0.295
Enlisted Groundcrew	1.31 (0.99,1.73)	0.061

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	158	49 (31.0)	1.05 (0.91,1.21)	0.506
Medium	159	57 (35.8)		
High	159	58 (36.5)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
473	0.98 (0.82,1.16)	0.785

[a] Relative risk for a twofold increase in initial dioxin.

Table 13-58. Analysis of Haptoglobin (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,194	337 (28.2)		
Background RH	376	115 (30.6)	1.13 (0.88,1.46)	0.338
Low RH	236	78 (33.1)	1.25 (0.93,1.69)	0.140
High RH	240	86 (35.8)	1.41 (1.05,1.89)	0.023
Low plus High RH	476	164 (34.5)	1.33 (1.06,1.67)	0.015

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,193		
Background RH	374	1.32 (1.01,1.72)	0.042
Low RH	235	1.25 (0.92,1.69)	0.160
High RH	238	1.15 (0.84,1.56)	0.382
Low plus High RH	473	1.19 (0.95,1.51)	0.136

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	283	86 (30.4)	1.03 (0.94,1.14)	0.509
Medium	285	88 (30.9)		
High	284	105 (37.0)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
847	0.91 (0.82,1.02)	0.107

[a] Relative risk for a twofold increase in 1987 dioxin.

No significant relation between initial dioxin and haptoglobin in its discrete form was revealed in either the unadjusted or adjusted Model 2 analyses (Table 13-58(c,d): p>0.50 for each analysis). The unadjusted Model 3 analysis of haptoglobin revealed significant differences between Ranch Hands and Comparisons for Ranch Hands in the high dioxin category and Ranch Hands in the low and high dioxin categories combined (Table 13-58(e): Est. RR=1.41, p=0.023; Est. RR=1.33, p=0.015, respectively). The adjusted Model 3 analysis showed a significant difference between Ranch Hands in the background dioxin category and Comparisons (Table 13-58(f): Adj. RR=1.32, p=0.042). The percentages of high haptoglobin values for Ranch Hands in the background dioxin category, Ranch Hands in the high dioxin category, Ranch Hands in the low and high dioxin categories combined, and Comparisons were 30.6, 35.8, 34.5, and 28.2, respectively. The unadjusted and adjusted Model 4 analyses were nonsignificant (Table 13-58(g,h): p>0.10 for each analysis).

13.2.2.3.50 Transferrin (Continuous)

The unadjusted and adjusted Model 1 analyses each revealed a significant overall group difference in the mean levels of transferrin (Table 13-59(a,b): difference of means=3.1 mg/dl, p=0.044, for the unadjusted analysis; difference of adjusted means=3.1 mg/dl, p=0.037, for the adjusted analysis). The adjusted mean level of transferrin was higher for the Ranch Hands than for the Comparisons (246.2 mg/dl vs. 243.1 mg/dl). Stratifying by occupation uncovered a marginally significant group difference within the enlisted groundcrew stratum in both the unadjusted and adjusted analyses (Table 13-59(a,b): difference of means=4.5 mg/dl, p=0.056, for the unadjusted analysis; difference of adjusted means=4.2 mg/dl, p=0.063, for the adjusted analysis). The adjusted mean level of transferrin among Ranch Hand enlisted groundcrew was 247.1 mg/dl versus 242.9 mg/dl among the Comparison enlisted groundcrew.

Table 13-59. Analysis of Transferrin (mg/dl) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***859***	***252.7***	***3.1 --***	***0.044***
	Comparison	***1,231***	***249.6***		
Officer	Ranch Hand	340	250.0	1.6 --	0.510
	Comparison	490	248.4		
Enlisted Flyer	Ranch Hand	150	254.5	3.0 --	0.439
	Comparison	185	251.5		
Enlisted Groundcrew	Ranch Hand	369	254.5	4.5 --	0.056
	Comparison	556	250.0		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 13-59. Analysis of Transferrin (Continuous) (mg/dl) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***854***	***246.2***	***3.1 --***	***0.037***
	Comparison	***1,229***	***243.1***		
Officer	Ranch Hand	340	243.5	1.9 --	0.412
	Comparison	489	241.6		
Enlisted Flyer	Ranch Hand	148	247.9	3.1 --	0.404
	Comparison	184	244.8		
Enlisted Groundcrew	Ranch Hand	366	247.1	4.2 --	0.063
	Comparison	556	242.9		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	158	251.5	251.5	0.001	0.003 (0.005)	0.594
Medium	159	254.8	254.8			
High	159	255.6	255.5			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of transferrin versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	158	247.6	0.014	–0.001 (0.006)	0.798
Medium	158	249.2			
High	157	249.2			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of transferrin versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 13-59. Analysis of Transferrin (Continuous) (mg/dl) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,194	249.5	249.5		
Background RH	376	250.9	250.9	1.4 --	0.480
Low RH	236	251.9	251.9	2.4 --	0.328
High RH	240	256.0	255.9	6.4 --	0.010
Low plus High RH	476	254.0	253.9	4.4 --	0.019

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,193	243.0		
Background RH	374	245.2	2.2 --	0.282
Low RH	235	246.1	3.1 --	0.200
High RH	238	247.9	4.9 --	0.050
Low plus High RH	473	247.0	4.0 --	0.032

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	251.0	0.004	0.005 (0.003)	0.082
Medium	285	251.4			
High	284	255.3			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of transferrin versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 13-59. Analysis of Transferrin (Continuous) (mg/dl) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	283	247.6	0.014	0.003 (0.004)	0.385
Medium	283	247.8			
High	281	249.9			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of transferrin versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

The unadjusted and adjusted Model 2 results were not significant (Table 13-59(c,d): p>0.59 for each analysis). The unadjusted Model 3 analysis revealed Ranch Hands in the high dioxin category and Ranch Hands in the low and high dioxin categories combined to be significantly different from Comparisons (Table 13-59(e): difference of means=6.4 mg/dl, p=0.010; difference of means=4.4 mg/dl, p=0.019, respectively). The adjusted analysis revealed the same two contrasts to be significant: Ranch Hands in the high dioxin category versus Comparisons and Ranch Hands in the low and high dioxin categories combined versus Comparisons (Table 13-59(f): difference of adjusted means=4.9 mg/dl, p=0.050; difference of adjusted means=4.0 mg/dl, p=0.032, respectively). The adjusted mean levels of transferrin for Ranch Hands in the high dioxin category, Ranch Hands in the low and high dioxin categories combined, and Comparisons were 247.9 mg/dl, 247.0 mg/dl, and 243.0 mg/dl, respectively.

A marginally significant association between 1987 dioxin and transferrin was shown in the unadjusted Model 4 analysis (Table 13-59(g): slope=0.005, p=0.082). After covariate adjustment, the results became nonsignificant (Table 13-59(h): p=0.385).

13.2.2.3.51 Transferrin (Discrete)

Both the unadjusted and adjusted Model 1 analyses of transferrin revealed a significant overall group difference between Ranch Hands and Comparisons (Table 13-60(a,b): Est. RR=0.73, p=0.036; Adj. RR=0.71, p=0.027, respectively). The percentage of low transferrin values among the Ranch Hands was 8.1 versus 10.9 for Comparisons. After stratifying by occupation, both the unadjusted and adjusted Model 1 analyses showed marginally significant differences between Ranch Hands and Comparisons within the officer stratum (Table 13-60(a,b): Est. RR=0.64, p=0.083; Adj. RR=0.63, p=0.070, respectively). The percentage of low transferrin values among Ranch Hand officers was 7.1 versus 10.6 among Comparison officers.

Table 13-60. Analysis of Transferrin (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Low	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***70 (8.1)***	***0.73 (0.54,0.98)***	***0.036***
	Comparison	***1,231***	***134 (10.9)***		
Officer	Ranch Hand	340	24 (7.1)	0.64 (0.39,1.06)	0.083
	Comparison	490	52 (10.6)		
Enlisted Flyer	Ranch Hand	150	15 (10.0)	0.87 (0.43,1.75)	0.691
	Comparison	185	21 (11.4)		
Enlisted Groundcrew	Ranch Hand	369	31 (8.4)	0.74 (0.47,1.17)	0.202
	Comparison	556	61 (11.0)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.71 (0.52,0.97)***	***0.027***
Officer	0.63 (0.38,1.04)	0.070
Enlisted Flyer	0.83 (0.41,1.68)	0.601
Enlisted Groundcrew	0.74 (0.47,1.18)	0.208

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Low	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	158	15 (9.5)	0.99 (0.77,1.27)	0.931
Medium	159	13 (8.2)		
High	159	11 (6.9)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
473	0.93 (0.69,1.24)	0.615

[a] Relative risk for a twofold increase in initial dioxin.

Table 13-60. Analysis of Transferrin (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	**n**	**Number (%) Low**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,194	133 (11.1)		
Background RH	376	31 (8.2)	0.72 (0.48,1.09)	0.121
Low RH	236	23 (9.7)	0.86 (0.54,1.37)	0.526
High RH	240	16 (6.7)	0.57 (0.33,0.97)	0.039
Low plus High RH	476	39 (8.2)	0.70 (0.48,1.02)	0.062

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Comparison	1,193		
Background RH	374	0.73 (0.48,1.11)	0.142
Low RH	235	0.78 (0.49,1.26)	0.311
High RH	238	0.57 (0.32,0.99)	0.045
Low plus High RH	473	0.66 (0.45,0.98)	0.039

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**	
1987 Dioxin	**n**	**Number (%) Low**	**Estimated Relative Risk (95% C.I.)[a]**	**p-Value**
Low	283	21 (7.4)	1.03 (0.88,1.22)	0.710
Medium	285	26 (9.1)		
High	284	23 (8.1)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
847	1.03 (0.85,1.24)	0.785

[a] Relative risk for a twofold increase in 1987 dioxin.

No significant association between initial dioxin and transferrin was found in the unadjusted or adjusted Model 2 analyses (Table 13-60(c,d): p>0.61 for each analysis). The unadjusted Model 3 analysis of transferrin revealed significant differences between Ranch Hands in the high dioxin category and Comparisons, as well as between Ranch Hands in the low and high dioxin categories combined and Comparisons (Table 13-60(e): Est. RR=0.57, p=0.039; Est. RR=0.70, p=0.062, respectively). The same contrasts were significant after adjusting for covariates (Table 13-60(f): Adj. RR=0.57, p=0.045, for Ranch Hands in the high dioxin category versus Comparisons; Adj. RR=0.66, p=0.039, for Ranch Hands in the low and high dioxin categories combined versus Comparisons). The percentages of low transferrin values among Ranch Hands in the high dioxin category, Ranch Hands in the low and high dioxin categories combined, and Comparisons were 6.7, 8.2, and 11.1, respectively. The unadjusted and adjusted Model 4 analyses were nonsignificant (Table 13-60(g,h): p>0.71 for each analysis).

13.2.3 Longitudinal Analysis

Longitudinal analyses were conducted on AST, ALT, GGT, cholesterol, HDL cholesterol, the cholesterol-HDL ratio, and triglycerides to examine whether changes across time differed with respect to group membership (Model 1), initial dioxin (Model 2), and categorized dioxin (Model 3). Model 4 was not examined in longitudinal analyses because 1987 dioxin, the measure of exposure in these models, changes over time and is not available for all participants for 1982 or 1997.

Discrete and continuous analyses were performed for all variables. The longitudinal analyses for all of these variables investigated the difference between the 1982 and 1997 examinations. These analyses were used to investigate the temporal effects of dioxin during the 15-year period between 1982 and 1997.

The longitudinal analysis for these variables in their continuous form examined the paired difference between the measurements from 1982 and 1997. These paired differences measured the change in these variables over time. Each of the three models used in the longitudinal analysis was adjusted for age and the dependent variable as measured in 1982 (see Chapter 7, Statistical Methods).

Participants who were abnormal in 1982 were not included in the longitudinal analysis of discrete dependent variables. The purpose of the longitudinal analysis was to examine the effects of dioxin exposure across time. Participants who were abnormal in 1982 were not considered to be at risk for developing the condition, because the condition already existed at the time of the first collection of data for the AFHS (1982). Only participants who were normal at the 1982 examination were considered to be at risk for developing the disease; therefore the rate of abnormalities under this restriction approximates an incidence rate between 1982 and 1997. That is, an incidence rate is a measure of the rate at which people without a condition develop the condition during a specified period of time (67). Summary statistics are provided for reference purposes for the 1985, 1987, and 1992 examinations.

The longitudinal analyses of discrete variables examined relative risks at the 1997 examination for participants who were classified as normal at the 1982 examination. The adjusted relative risks estimated from each of the three models were used to investigate the change in the dependent variable over time. All three models were adjusted for age; Models 2 and 3 also were adjusted for the percentage of body fat at the time of the blood measurement of dioxin.

The cutpoints for all of these variables except the cholesterol-HDL ratio differed between examinations. The cutpoints changed between examinations because a different laboratory was used to perform the analysis or because an upgrade in the equipment used caused a change in the reference values. This upgrade in equipment may have affected the mean level or the percent abnormal for the dependent variable between examinations. These cutpoints were used for determining abnormal and normal classifications for each of the respective examinations and are shown in Table 13-61.

Table 13-61. Normal Ranges from Air Force Health Study Examinations for Dependent Variables Used in Longitudinal Analysis

Dependent Variable (Units)	Examination 1982	1985	1987	1992	1997
AST (U/l)	≤41	≤47	≤47	≤50	≤37
ALT (U/l)	≤45	≤36	≤36	≤55	≤65
GGT (U/l)	≤85	≤85	≤85	≤51	≤85
Cholesterol (mg/dl)	≤240 (Age <40) ≤265 (Age ≥40)	≤250 (Age <45) ≤260 (Age 45–69) ≤250 (Age ≥70)	≤250 (Age <45) ≤260 (Age 45–69) ≤250 (Age ≥70)	≤250 (Age <45) ≤260 (Age 45–69) ≤250 (Age ≥70)	≤260 (Age <50) ≤250 (Age ≥50)[a]
HDL (mg/dl)	≥25 (Age <50) ≥32 (Age ≥50)	≥30 (Age <40) ≥25 (Age 40–44) ≥30 (Age ≥45)	≥30 (Age <40) ≥25 (Age 40–44) ≥30 (Age ≥45)	≥30 (Age <40) ≥25 (Age 40–44) ≥30 (Age ≥45)	≥32
Triglycerides (mg/dl)	≤150 (Age <40) ≤160 (Age 40–49) ≤190 (Age ≥50)	≤320 (Age <55) ≤290 (Age 55–64) ≤260 (Age ≥65)	≤320 (Age <55) ≤290 (Age 55–64) ≤260 (Age ≥65)	≤320 (Age <55) ≤290 (Age 55–64) ≤260 (Age ≥65)	≤200

[a] Cutpoint lower for cholesterol for older participants per manufacturer's recommendation.

13.2.3.1 Laboratory Examination Variables

13.2.3.1.1 AST (Continuous)

The analyses in each of Models 1 through 3 did not reveal a significant association between dioxin and the change in mean AST levels between 1982 and 1997 (Table 13-62(a–c): p>0.37 for each analysis).

Table 13-62. Longitudinal Analysis of AST (U/I) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Mean[a]/(n) Examination 1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	***Ranch Hand***	***32.61 (804)***	***33.33 (787)***	***25.50 (778)***	***23.03 (778)***	***22.99 (804)***	***–9.62***	***–0.03***	***0.859***
	Comparison	***32.48 (956)***	***33.47 (938)***	***25.34 (929)***	***23.59 (933)***	***22.89 (956)***	***–9.59***		
Officer	Ranch Hand	32.69 (309)	34.01 (304)	25.85 (301)	23.69 (300)	23.29 (309)	–9.40	0.15	0.897
	Comparison	32.86 (377)	33.57 (371)	25.76 (363)	24.00 (370)	23.31 (377)	–9.55		
Enlisted Flyer	Ranch Hand	31.89 (146)	32.24 (143)	24.47 (141)	21.14 (143)	22.19 (146)	–9.69	0.47	0.710
	Comparison	33.02 (142)	33.53 (141)	25.10 (140)	23.30 (138)	22.87 (142)	–10.16		
Enlisted Groundcrew	Ranch Hand	32.84 (349)	33.18 (340)	25.63 (336)	23.28 (335)	23.06 (349)	–9.78	–0.34	0.687
	Comparison	31.98 (437)	33.36 (426)	25.08 (426)	23.32 (425)	22.54 (437)	–9.44		

[a] Transformed from natural logarithm scale.

[b] Difference between 1997 and 1982 examination means after transformation to original scale.

[c] P-value is based on analysis of natural logarithm of AST; results adjusted for natural logarithm of AST in 1982 and age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

Table 13-62. Longitudinal Analysis of AST (U/l) (Continuous) (Continued)

(b) MODEL 2: RANCH HANDS – INITIAL DIOXIN							
Initial Dioxin Category Summary Statistics						Analysis Results for Log_2 (Initial Dioxin)[b]	
	Mean[a]/(n) Examination						
Initial Dioxin	1982	1985	1987	1992	1997	Adjusted Slope (Std. Error)	p-Value
Low	33.11 (151)	34.06 (147)	25.46 (150)	22.57 (146)	23.39 (151)	−0.004 (0.012)	0.731
Medium	33.39 (156)	34.46 (154)	26.08 (152)	23.18 (152)	23.64 (156)		
High	33.54 (151)	33.33 (148)	25.86 (146)	23.82 (148)	23.56 (151)		

[a] Transformed from natural logarithm scale.
[b] Results based on difference between natural logarithm of 1997 AST and natural logarithm of 1982 AST versus $\log_2$ (initial dioxin); results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of 1982 AST, and age in 1997.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY								
	Mean[a]/(n) Examination							
Dioxin Category	1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
Comparison	32.46 (929)	33.50 (913)	25.35 (903)	23.54 (907)	22.87 (929)	−9.59		
Background RH	31.70 (340)	32.54 (333)	25.13 (325)	22.78 (327)	22.22 (340)	−9.48	0.11	0.574
Low RH	32.75 (226)	34.41 (220)	25.59 (222)	23.05 (218)	23.40 (226)	−9.34	0.25	0.373
High RH	33.94 (232)	33.51 (229)	26.00 (226)	23.32 (228)	23.65 (232)	−10.29	−0.70	0.911
Low plus High RH	33.35 (458)	33.95 (449)	25.80 (448)	23.19 (446)	23.53 (458)	9.82	−0.23	0.520

[a] Transformed from natural logarithm scale.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of natural logarithm of 1997 AST; results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of 1982 AST, and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

13.2.3.1.2 AST (Discrete)

All longitudinal analyses of the participants with high AST levels in 1997 that were normal in 1982 were nonsignificant (Table 13-63(a–c): p>0.15 for each analysis).

Table 13-63. Longitudinal Analysis of AST (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) High/(n) Examination 1982	1985	1987	1992	1997
All	***Ranch Hand***	***99 (12.3) (804)***	***51 (6.5) (787)***	***31 (4.0) (778)***	***21 (2.7) (778)***	***60 (7.5) (804)***
	Comparison	***122 (12.8) (956)***	***70 (7.5) (938)***	***26 (2.8) (929)***	***31 (3.3) (933)***	***60 (6.3) (956)***
Officer	Ranch Hand	34 (11.0) (309)	24 (7.9) (304)	14 (4.7) (301)	11(3.7) (300)	21 (6.8) (309)
	Comparison	52 (13.8) (377)	24 (6.5) (371)	13 (3.6) (363)	14 (3.8) (370)	23 (6.1) (377)
Enlisted Flyer	Ranch Hand	16 (11.0) (146)	7 (4.9) (143)	4 (2.8) (141)	1 (0.7) (143)	10 (6.8) (146)
	Comparison	20 (14.1) (142)	13 (9.2) (141)	5 (3.6) (140)	6 (4.3) (138)	12 (8.5) (142)
Enlisted Groundcrew	Ranch Hand	49 (14.0) (349)	20 (5.9) (340)	13 (3.9) (336)	9 (2.7) (335)	29 (8.3) (349)
	Comparison	50 (11.4) (437)	33 (7.7) (426)	8 (1.9) (426)	11 (2.6) (425)	25 (5.7) (437)

Occupational Category	Group	Normal in 1982: n in 1997	Normal in 1982: Number (%) High in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***705***	***35 (5.0)***	***1.13 (0.70,1.81)***	***0.614***
	Comparison	***834***	***37 (4.4)***		
Officer	Ranch Hand	275	11 (4.0)	0.87 (0.39,1.93)	0.735
	Comparison	325	15 (4.6)		
Enlisted Flyer	Ranch Hand	130	6 (4.6)	0.69 (0.23,2.05)	0.506
	Comparison	122	8 (6.6)		
Enlisted Groundcrew	Ranch Hand	300	18 (6.0)	1.68 (0.82,3.45)	0.153
	Comparison	387	14 (3.6)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal AST level in 1982 (see Chapter 7, Statistical Methods).

Table 13-63. Longitudinal Analysis of AST (Discrete) (Continued)

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN

Initial Dioxin	Number (%) High/(n) Examination 1982	1985	1987	1992	1997
Low	17 (11.3) (151)	11 (7.5) (147)	6 (4.0) (150)	4 (2.7) (146)	11 (7.3) (151)
Medium	30 (19.2) (156)	11 (7.1) (154)	4 (2.6) (152)	4 (2.6) (152)	20 (12.8) (156)
High	23 (15.2) (151)	11 (7.4) (148)	7 (4.8) (146)	4 (2.7) (148)	14 (9.3) (151)

Initial Dioxin Category Summary Statistics: Initial Dioxin	Normal in 1982: n in 1997	Normal in 1982: Number (%) High in 1997	Analysis Results for Log_2 (Initial Dioxin)[a]: Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	134	6 (4.5)	1.18 (0.87,1.59)	0.297
Medium	126	11 (8.7)		
High	128	9 (7.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal AST level in 1982 (see Chapter 7, Statistical Methods).

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY

Dioxin Category	Number (%) High/(n) Examination 1982	1985	1987	1992	1997
Comparison	118 (12.7) (929)	69 (7.6) (913)	25 (2.8) (903)	30 (3.3) (907)	59 (6.4) (929)
Background RH	27 (7.9) (340)	18 (5.4) (333)	14 (4.3) (325)	9 (2.8) (327)	14 (4.1) (340)
Low RH	26 (11.5) (226)	19 (8.6) (220)	9 (4.1) (222)	8 (3.7) (218)	19 (8.4) (226)
High RH	44 (19.0) (232)	14 (6.1) (229)	8 (3.5) (226)	4 (1.8) (228)	26 (11.2) (232)
Low plus High RH	70 (15.3) (458)	33 (7.3) (449)	17 (3.8) (448)	12 (2.7) (446)	45 (9.8) (458)

Table 13-63. Longitudinal Analysis of AST (Discrete) (Continued)

Dioxin Category	Normal in 1982 n in 1997	Normal in 1982 Number (%) High in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	811	37 (4.6)		
Background RH	313	8 (2.6)	0.59 (0.27,1.30)	0.193
Low RH	200	12 (6.0)	1.34 (0.68,2.63)	0.395
High RH	188	14 (7.4)	1.58 (0.83,3.00)	0.166
Low plus High RH	388	26 (6.7)	1.45 (0.86,2.44)	0.162

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal AST level in 1982 (see Chapter 7, Statistical Methods).

13.2.3.1.3 ALT (Continuous)

Models 1 and 2 of the longitudinal analyses of ALT in its continuous form revealed no significant association between the change in mean AST levels and dioxin (Table 13-64(a,b): p>0.21). Model 3 analysis of the change in mean ALT levels between 1982 and 1997 revealed two marginally significant contrasts: Ranch Hands in the low dioxin category versus Comparisons and Ranch Hands in the low and high dioxin categories combined versus Comparisons (Table 13-64(c): difference of examination mean change=1.02 U/l, p=0.054; difference of examination mean change=0.72 U/l, p=0.094, respectively). The examination mean changes for Ranch Hands in the low dioxin category, Ranch Hands in the low and high dioxin categories combined, and Comparisons were 22.84 U/l, 22.54 U/l, and 21.82 U/l, respectively.

Table 13-64. Longitudinal Analysis of ALT (U/l) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS										
		Mean[a]/(n) Examination								
Occupational Category	Group	1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	***Ranch Hand***	*19.84*	*21.66*	*20.52*	*27.12*	*42.55*	*22.71*	*0.89*	*0.214*
		(804)	*(787)*	*(778)*	*(778)*	*(804)*			
	Comparison	*20.38*	*22.53*	*20.49*	*27.91*	*42.20*	*21.82*		
		(956)	*(938)*	*(929)*	*(933)*	*(956)*			
Officer	Ranch Hand	19.71	21.96	20.53	27.01	41.93	22.22	0.99	0.295
		(309)	(304)	(301)	(300)	(309)			
	Comparison	20.32	21.97	20.35	27.39	41.55	21.23		
		(377)	(371)	(363)	(370)	(377)			
Enlisted Flyer	Ranch Hand	18.69	20.85	19.83	25.15	41.33	22.63	0.77	0.910
		(146)	(143)	(141)	(143)	(146)			
	Comparison	20.59	22.01	19.84	28.03	42.45	21.86		
		(142)	(141)	(140)	(138)	(142)			
Enlisted Groundcrew	Ranch Hand	20.46	21.73	20.79	28.10	43.63	23.17	0.85	0.377
		(349)	(340)	(336)	(335)	(349)			
	Comparison	20.37	23.20	20.82	28.33	42.69	22.32		
		(437)	(426)	(426)	(425)	(437)			

[a] Transformed from natural logarithm scale.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of natural logarithm of ALT; results adjusted for natural logarithm of ALT in 1982 and age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

Table 13-64. Longitudinal Analysis of ALT (U/l) (Continuous) (Continued)

(b) MODEL 2: RANCH HANDS – INITIAL DIOXIN							
Initial Dioxin Category Summary Statistics						Analysis Results for Log_2 (Initial Dioxin)[b]	
	Mean[a]/(n) Examination						
Initial Dioxin	1982	1985	1987	1992	1997	Adjusted Slope (Std. Error)	p-Value
Low	20.29 (151)	22.08 (147)	20.15 (150)	26.54 (146)	42.36 (151)	–0.007 (0.010)	0.444
Medium	21.76 (156)	24.10 (154)	21.94 (152)	28.72 (152)	44.95 (156)		
High	22.96 (151)	23.82 (148)	23.07 (146)	30.13 (148)	45.27 (151)		

[a] Transformed from natural logarithm scale.
[b] Results based on difference between natural logarithm of 1997 ALT and natural logarithm of 1982 ALT versus $\log_2$ (initial dioxin); results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of 1982 ALT, and age in 1997.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY								
	Mean[a]/(n) Examination							
Dioxin Category	1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
Comparison	20.34 (929)	22.49 (913)	20.46 (903)	27.87 (907)	42.16 (929)	21.82		
Background RH	17.53 (340)	19.62 (33)	19.01 (325)	25.36 (327)	40.39 (340)	22.87	1.05	0.751
Low RH	20.46 (226)	23.08 (220)	20.50 (222)	27.51 (218)	43.30 (226)	22.84	1.02	0.054
High RH	22.86 (232)	23.57 (229)	22.90 (226)	29.36 (228)	45.07 (232)	22.20	0.38	0.503
Low plus High RH	21.64 (458)	23.33 (449)	21.67 (448)	28.44 (446)	44.18 (458)	22.54	0.72	0.094

[a] Transformed from natural logarithm scale.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of natural logarithm of 1997 ALT; results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of 1982 ALT, and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

13.2.3.1.4 ALT (Discrete)

Examination of Models 1 and 2 of the longitudinal analyses for discretized ALT did not find a significant association between dioxin and the percentage of participants with normal ALT values in 1982 and high ALT values in 1997 (Table 13-65(a,b): p>0.19 for each analysis).

Table 13-65. Longitudinal Analysis of ALT (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) High/(n) Examination 1982	1985	1987	1992	1997
All	***Ranch Hand***	***59 (7.3) 804***	***107 (13.6) (787)***	***92 (11.8) (778)***	***45 (5.8) (778)***	***65 (8.1) (804)***
	Comparison	***67 (7.0) (956)***	***133 (14.2) (938)***	***92 (9.9) (929)***	***64 (6.9) (933)***	***68 (7.1) (956)***
Officer	Ranch Hand	23 (7.4) (309)	46 (15.1) (304)	38 (12.6) (301)	19 (6.3) (300)	20 (6.5) (309)
	Comparison	26 (6.9) (377)	45 (12.1) (371)	39 (10.7) (363)	20 (5.4) (370)	16 (4.2) (377)
Enlisted Flyer	Ranch Hand	10 (6.8) (146)	15 (10.5) (143)	14 (9.9) (141)	7 (4.9) (143)	15 (10.3) (146)
	Comparison	11 (7.7) (142)	19 (13.5) (141)	9 (6.4) (140)	11 (8.0) (138)	15 (10.6) (142)
Enlisted Groundcrew	Ranch Hand	26 (7.4) (349)	46 (13.5) (340)	40 (11.9) (336)	19 (5.7) (335)	30 (8.6) (349)
	Comparison	30 (6.9) (437)	69 (16.2) (426)	44 (10.3) (426)	33 (7.8) (425)	37 (8.5) (437)

Occupational Category	Group	Normal in 1982: n in 1997	Number (%) High in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***745***	***43 (5.8)***	***0.92 (0.61,1.39)***	***0.690***
	Comparison	***889***	***56 (6.3)***		
Officer	Ranch Hand	286	14 (4.9)	1.53 (0.70,3.39)	0.289
	Comparison	351	12 (3.4)		
Enlisted Flyer	Ranch Hand	136	11 (8.1)	0.87 (0.37,2.06)	0.749
	Comparison	131	12 (9.2)		
Enlisted Groundcrew	Ranch Hand	323	18 (5.6)	0.67 (0.37,1.23)	0.195
	Comparison	407	32 (7.9)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal ALT level in 1982 (see Chapter 7, Statistical Methods).

Table 13-65. Longitudinal Analysis of ALT (Discrete) (Continued)

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN

Initial Dioxin	Number (%) High/(n) Examination 1982	1985	1987	1992	1997
Low	12 (7.9) (151)	20 (13.6) (147)	11 (7.3) (150)	4 (2.7) (146)	10 (6.6) (151)
Medium	10 (6.4) (156)	21 (13.6) (154)	22 (14.5) (152)	13 (8.6) (152)	21 (13.5) (156)
High	19 (12.6) (151)	27 (18.2) (148)	22 (15.1) (146)	13 (8.8) (148)	19 (12.6) (151)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1982			
Initial Dioxin	n in 1997	Number (%) High in 1997	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	139	8 (5.8)	1.05 (0.78,1.40)	0.750
Medium	146	14 (9.6)		
High	132	10 (7.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal ALT level in 1982 (see Chapter 7, Statistical Methods).

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY

Dioxin Category	Number (%) High/(n) Examination 1982	1985	1987	1992	1997
Comparison	65 (7.0) (929)	129 (14.1) (913)	90 (10.0) (903)	60 (6.6) (907)	67 (7.2) (929)
Background RH	17 (5.0) (340)	38 (11.4) (333)	36 (11.1) (325)	14 (4.3) (327)	14 (4.1) (340)
Low RH	17 (7.5) (226)	30 (13.6) (220)	21 (9.5) (222)	10 (4.6) (218)	20 (8.8) (226)
High RH	24 (10.3) (232)	38 (16.6) (229)	34 (15.0) (226)	20 (8.8) (228)	30 (12.9) (232)
Low plus High RH	41 (9.0) (458)	68 (15.1) (449)	55 (12.3) (448)	30 (6.7) (446)	50 (10.9) (458)

Table 13-65. Longitudinal Analysis of ALT (Discrete) (Continued)

Dioxin Category	Normal in 1982: n in 1997	Normal in 1982: Number (%) High in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	864	56 (6.5)		
Background RH	323	10 (3.1)	0.55 (0.27,1.10)	0.089
Low RH	209	15 (7.2)	1.23 (0.68,2.24)	0.495
High RH	208	17 (8.2)	1.04 (0.59,1.85)	0.889
Low plus High RH	417	32 (7.7)	1.13 (0.72,1.79)	0.591

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had an normal ALT level in 1982 (see Chapter 7, Statistical Methods).

The Model 3 analysis of the percentage of participants with high ALT levels in 1997 and normal ALT levels in 1982 revealed a marginally significant difference between Ranch Hands in the background dioxin category and Comparisons (Table 13-65(c): Adj. RR=0.55, p=0.089). Of the Comparisons with normal ALT levels in 1982, 6.5 percent had high ALT levels in 1997, whereas 3.1 percent of Ranch Hands in the background dioxin category with normal ALT levels in 1982 had high ALT levels in 1997.

13.2.3.1.5 GGT (Continuous)

The analyses in each of Models 1 through 3 did not reveal a significant association between dioxin and the change in mean GGT levels (Table 13-66(a–c): p>0.26 for each analysis).

Table 13-66. Longitudinal Analysis of GGT (U/l) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS										
		Mean[a]/(n) Examination								
Occupational Category	Group	1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	***Ranch Hand***	***38.12 (804)***	***31.57 (787)***	***32.05 (778)***	***32.38 (778)***	***43.70 (804)***	***5.57***	***0.74***	***0.266***
	Comparison	***37.44 (955)***	***31.53 (937)***	***31.30 (928)***	***31.61 (932)***	***42.27 (955)***	***4.83***		
Officer	Ranch Hand	36.62 (309)	30.88 (304)	31.40 (301)	31.54 (300)	42.13 (309)	5.51	0.41	0.567
	Comparison	36.09 (377)	30.25 (371)	30.70 (363)	31.24 (370)	41.19 (377)	5.10		
Enlisted Flyer	Ranch Hand	38.58 (146)	31.70 (143)	31.74 (141)	30.77 (143)	44.65 (146)	6.07	1.99	0.698
	Comparison	41.81 (142)	34.81 (141)	33.64 (140)	34.67 (138)	45.89 (142)	4.08		
Enlisted Groundcrew	Ranch Hand	39.31 (349)	32.13 (340)	32.77 (336)	33.88 (335)	44.73 (349)	5.42	0.61	0.442
	Comparison	37.28 (436)	31.63 (425)	31.08 (425)	30.99 (424)	42.09 (436)	4.81		

[a] Transformed from natural logarithm scale.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of natural logarithm of GGT; results adjusted for natural logarithm of GGT in 1982 and age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

Table 13-66. Longitudinal Analysis of GGT (U/l) (Continuous) (Continued)

(b) MODEL 2: RANCH HANDS – INITIAL DIOXIN

Initial Dioxin Category Summary Statistics						Analysis Results for Log_2 (Initial Dioxin)[b]	
	Mean[a]/(n) Examination						
Initial Dioxin	1982	1985	1987	1992	1997	Adjusted Slope (Std. Error)	p-Value
Low	41.42 (151)	33.83 (147)	32.52 (150)	32.74 (146)	43.50 (151)	–0.009 (0.017)	0.579
Medium	42.17 (156)	35.47 (154)	36.50 (152)	36.72 (152)	48.93 (156)		
High	41.69 (151)	33.53 (148)	34.54 (146)	35.61 (148)	46.45 (151)		

[a] Transformed from natural logarithm scale.
[b] Results based on difference between natural logarithm of 1997 GGT and natural logarithm of 1982 GGT versus $\log_2$ (initial dioxin); results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of 1982 GGT, and age in 1997.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY

Dioxin Category	Mean[a]/(n) Examination 1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
Comparison	37.10 (928)	31.17 (912)	30.95 (902)	31.19 (906)	41.92 (928)	4.82		
Background RH	33.22 (340)	28.00 (333)	28.71 (325)	28.90 (327)	39.90 (340)	6.69	1.87	0.363
Low RH	40.41 (226)	33.57 (220)	32.97 (222)	33.56 (218)	44.00 (226)	3.58	–1.24	0.686
High RH	43.12 (232)	34.98 (229)	36.05 (226)	36.45 (228)	48.59 (232)	5.48	0.66	0.276
Low plus High RH	41.76 (458)	34.28 (449)	34.49 (448)	35.01 (446)	46.27 (458)	4.51	–0.31	0.330

[a] Transformed from natural logarithm scale.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of natural logarithm of 1997 GGT; results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of 1982 GGT, and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

13.2.3.1.6 GGT (Discrete)

The longitudinal analyses in Models 1 through 3 did not reveal a significant association between the change in discretized GGT values and dioxin (Table 13-67(a–c): $p>0.10$).

Table 13-67. Longitudinal Analysis of GGT (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) High/(n) Examination 1982	1985	1987	1992	1997
All	***Ranch Hand***	***68 (8.5) (804)***	***58 (7.4) (787)***	***57 (7.3) (778)***	***155 (19.9) (778)***	***84 (10.4) (804)***
	Comparison	***81 (8.5) (955)***	***76 (8.1) (937)***	***60 (6.5) (928)***	***163 (17.5) (932)***	***94 (9.8) (955)***
Officer	Ranch Hand	26 (8.4) (309)	21 (6.9) (304)	24 (8.0) (301)	56 (18.7) (300)	27 (8.7) (309)
	Comparison	31 (8.2) (377)	27 (7.3) (371)	23 (6.3) (363)	64 (17.3) (370)	32 (8.5) (377)
Enlisted Flyer	Ranch Hand	15 (10.3) (146)	11 (7.7) (143)	13 (9.2) (141)	25 (17.5) (143)	23 (15.8) (146)
	Comparison	16 (11.3) (142)	17 (12.1) (141)	15 (10.7) (140)	29 (21.0) (138)	21 (14.8) (142)
Enlisted Groundcrew	Ranch Hand	27 (7.7) (349)	26 (7.6) (340)	20 (6.0) (336)	74 (22.1) (335)	34 (9.7) (349)
	Comparison	34 (7.8) (436)	32 (7.5) (425)	22 (5.2) (425)	70 (16.5) (424)	41 (9.4) (436)

Occupational Category	Group	Normal in 1982: n in 1997	Number (%) High in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***736***	***48 (6.5)***	***1.02 (0.69,1.53)***	***0.909***
	Comparison	***874***	***56 (6.4)***		
Officer	Ranch Hand	283	13 (4.6)	1.01 (0.48,2.14)	0.982
	Comparison	346	16 (4.6)		
Enlisted Flyer	Ranch Hand	131	16 (12.2)	1.12 (0.52,2.41)	0.768
	Comparison	126	14 (11.1)		
Enlisted Groundcrew	Ranch Hand	322	19 (5.9)	0.90 (0.49,1.66)	0.731
	Comparison	402	26 (6.5)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal GGT level in 1982 (see Chapter 7, Statistical Methods).

Table 13-67. Longitudinal Analysis of GGT (Discrete) (Continued)

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN

Initial Dioxin	Number (%) High/(n) Examination 1982	1985	1987	1992	1997
Low	17 (11.3) 151	12 (8.2) (147)	10 (6.7) (150)	26 (17.8) (146)	16 (10.6) (151)
Medium	15 (9.6) (156)	12 (7.8) (154)	14 (9.2) (152)	39 (25.7) (152)	27 (17.3) (156)
High	17 (11.3) (151)	14 (9.5) (148)	13 (8.9) (146)	33 (22.3) (148)	17 (11.3) (151)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1982			
Initial Dioxin	n in 1997	Number (%) High in 1997	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	134	8 (6.0)	1.03 (0.78,1.35)	0.860
Medium	141	19 (13.5)		
High	134	8 (6.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal GGT level in 1982 (see Chapter 7, Statistical Methods).

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY

Dioxin Category	Number (%) High/(n) Examination 1982	1985	1987	1992	1997
Comparison	74 (8.0) (928)	71 (7.8) (912)	55 (6.1) (902)	151 (16.7) (906)	89 (9.6) (928)
Background RH	17 (5.0) (340)	19 (5.7) (333)	19 (5.8) (325)	55 (16.8) (327)	22 (6.5) (340)
Low RH	22 (9.7) (226)	16 (7.3) (220)	15 (6.8) (222)	43 (19.7) (218)	27 (11.9) (226)
High RH	27 (11.6) (232)	22 (9.6) (229)	22 (9.7) (226)	55 (24.1) (228)	33 (14.2) (232)
Low plus High RH	49 (10.7) (458)	38 (8.5) (449)	37 (8.3) (448)	98 (22.0) (446)	60 (13.1) (458)

Table 13-67. Longitudinal Analysis of GGT (Discrete) (Continued)

	Normal in 1982			
Dioxin Category	n in 1997	Number (%) High in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	854	55 (6.4)		
Background RH	323	12 (3.7)	0.58 (0.31,1.11)	0.101
Low RH	204	15 (7.4)	1.19 (0.66,2.16)	0.569
High RH	205	20 (9.8)	1.46 (0.85,2.52)	0.173
Low plus High RH	409	35 (8.6)	1.32 (0.84,2.06)	0.224

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal GGT level in 1982 (see Chapter 7, Statistical Methods).

13.2.3.1.7 Cholesterol (Continuous)

The Model 1 analysis of the change in mean cholesterol levels did not uncover a significant difference between overall Ranch Hands and Comparisons (Table 13-68(a): p=0.877). Stratifying by occupation showed marginally significant group differences in the officers and enlisted groundcrew strata (Table 13-68(a): difference of examination mean change =–3.8 mg/dl, p=0.075, for officers; difference of examination mean change=6.5 mg/dl, p=0.082, for enlisted groundcrew). Among the officers, the Ranch Hand mean decreased by 6.5 mg/dl between 1982 and 1997 versus a mean decrease of 2.7 mg/dl for Comparisons. Among the enlisted groundcrew, the Ranch Hands had a mean increase of 4.0 mg/dl between 1982 and 1997 versus a mean decrease of 2.5 mg/dl for Comparisons. Model 2 and 3 analyses did not show any significant relations between dioxin and the change in mean cholesterol levels (Table 13-68(b,c): p>0.12 for each analysis).

Table 13-68. Longitudinal Analysis of Cholesterol (mg/dl) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Mean[a]/(n) Examination 1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	***Ranch Hand***	***212.3 (804)***	***214.9 (787)***	***216.0 (778)***	***215.9 (778)***	***210.8 (804)***	***–1.5***	***2.0***	***0.877***
	Comparison	***215.8 (956)***	***217.2 (938)***	***215.8 (929)***	***216.0 (933)***	***212.4 (956)***	***–3.5***		
Officer	Ranch Hand	212.2 (309)	215.4 (304)	215.9 (301)	214.3 (300)	205.7 (309)	–6.5	–3.8	0.075
	Comparison	213.6 (377)	215.2 (371)	214.6 (363)	213.0 (370)	210.8 (377)	–2.7		
Enlisted Flyer	Ranch Hand	217.4 (146)	220.0 (143)	218.6 (141)	219.8 (143)	213.5 (146)	–3.9	4.4	0.838
	Comparison	224.7 (142)	222.5 (141)	221.8 (140)	221.8 (138)	216.4 (142)	–8.3		
Enlisted Groundcrew	Ranch Hand	210.3 (349)	212.4 (340)	214.9 (336)	215.8 (335)	214.3 (349)	4.0	6.5	0.082
	Comparison	214.9 (437)	217.3 (426)	214.9 (426)	216.9 (425)	212.4 (437)	–2.5		

[a] Transformed from square root scale.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of square root of cholesterol; results adjusted for square root of cholesterol in 1982 and age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

Table 13-68. Longitudinal Analysis of Cholesterol (mg/dl) (Continuous) (Continued)

(b) MODEL 2: RANCH HANDS – INITIAL DIOXIN							
Initial Dioxin Category Summary Statistics						Analysis Results for Log_2 (Initial Dioxin)[b]	
	Mean[a]/(n) Examination						
Initial Dioxin	1982	1985	1987	1992	1997	Adjusted Slope (Std. Error)	p-Value
Low	213.4 (151)	216.4 (147)	216.9 (150)	215.5 (146)	205.6 (151)	0.063 (0.041)	0.128
Medium	212.5 (156)	215.7 (154)	217.0 (152)	215.8 (152)	213.8 (156)		
High	218.6 (151)	219.0 (148)	219.0 (146)	220.8 (148)	217.9 (151)		

[a] Transformed from square root scale.
[b] Results based on difference between square root of 1997 cholesterol and square root of 1982 cholesterol versus $\log_2$ (initial dioxin); results adjusted for percent body fat at the date of the blood measurement of dioxin, square root of 1982 cholesterol, and age in 1997.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY								
	Mean[a]/(n) Examination							
Dioxin Category	1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
Comparison	215.5 (929)	217.2 (913)	215.7 (903)	215.8 (907)	212.3 (929)	–3.2		
Background RH	208.9 (340)	212.1 (333)	214.0 (325)	214.1 (327)	208.8 (340)	–0.1	3.1	0.800
Low RH	212.8 (226)	215.8 (220)	215.7 (222)	216.4 (218)	208.0 (226)	–4.8	–1.6	0.410
High RH	216.7 (232)	218.2 (229)	219.5 (226)	218.2 (228)	216.7 (232)	0.0	3.2	0.168
Low plus High RH	214.8 (458)	217.0 (449)	217.6 (448)	217.3 (446)	212.4 (458)	–2.4	0.8	0.704

[a] Transformed from square root scale.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of square root of 1997 cholesterol; results adjusted for percent body fat at the date of the blood measurement of dioxin, square root of 1982 cholesterol, and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

13.2.3.1.8 Cholesterol (Discrete)

The Model 1 analysis of the percentage of participants with high cholesterol levels in 1997 did not uncover a significant difference between overall Ranch Hands and Comparisons (Table 13-69(a): p=0.323). Stratifying by occupation showed a significant group difference in the enlisted groundcrew stratum (Table 13-69(a): Adj. RR=1.68, p=0.031). For enlisted groundcrew with normal cholesterol levels in 1982, 15.6 percent of the Ranch Hands and 9.9 percent of the Comparisons had high cholesterol levels in 1997.

Table 13-69. Longitudinal Analysis of Cholesterol (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) High/(n) Examination 1982	1985	1987	1992	1997
All	***Ranch Hand***	***121 (15.0) (804)***	***127 (16.1) (787)***	***131 (16.8) (778)***	***108 (13.9) (778)***	***121 (15.0) (804)***
	Comparison	***156 (16.3) (956)***	***170 (18.1) (938)***	***135 (14.5) (929)***	***121 (13.0) (933)***	***142 (14.9) (956)***
Officer	Ranch Hand	34 (11.0) (309)	49 (16.1) (304)	49 (16.3) (301)	35 (11.7) (300)	36 (11.7) (309)
	Comparison	43 (11.4) (377)	53 (14.3) (371)	43 (11.8) (363)	40 (10.8) (370)	53 (14.1) (377)
Enlisted Flyer	Ranch Hand	27 (18.5) (146)	27 (18.9) (143)	30 (21.3) (141)	26 (18.2) (143)	21 (14.4) (146)
	Comparison	29 (20.4) (142)	34 (24.1) (141)	27 (19.3) (140)	19 (13.8) (138)	21 (14.8) (142)
Enlisted Groundcrew	Ranch Hand	60 (17.2) (349)	51 (15.0) (340)	52 (15.5) (336)	47 (14.0) (335)	64 (18.3) (349)
	Comparison	84 (19.2) (437)	83 (19.5) (426)	65 (15.3) (426)	62 (14.6) (425)	68 (15.6) (437)

Occupational Category	Group	Normal in 1982: n in 1997	Number (%) High in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***683***	***81 (11.9)***	***1.18 (0.85,1.63)***	***0.323***
	Comparison	***800***	***82 (10.3)***		
Officer	Ranch Hand	275	25 (9.1)	0.83 (0.48,1.41)	0.483
	Comparison	334	36 (10.8)		
Enlisted Flyer	Ranch Hand	119	11 (9.2)	0.94 (0.39,2.27)	0.896
	Comparison	113	11 (9.7)		
Enlisted Groundcrew	Ranch Hand	289	45 (15.6)	1.68 (1.05,2.70)	0.031
	Comparison	353	35 (9.9)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal cholesterol level in 1982 (see Chapter 7, Statistical Methods).

Table 13-69. Longitudinal Analysis of Cholesterol (Discrete) (Continued)

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN

Initial Dioxin	Number (%) High/(n) Examination 1982	1985	1987	1992	1997
Low	18 (11.9) (151)	25 (17.0) (147)	25 (16.7) (150)	19 (13.0) (146)	18 (11.9) (151)
Medium	24 (15.4) (156)	25 (16.2) (154)	23 (15.1) (152)	21 (13.8) (152)	29 (18.6) (156)
High	39 (25.8) (151)	26 (17.6) (148)	23 (15.8) (146)	27 (18.2) (148)	30 (19.9) (151)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1982			
Initial Dioxin	n in 1997	Number (%) High in 1997	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	133	14 (10.5)	1.23 (0.98,1.54)	0.072
Medium	132	21 (15.9)		
High	112	20 (17.9)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal cholesterol level in 1982 (see Chapter 7, Statistical Methods).

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY

Dioxin Category	Number (%) High/(n) Examination 1982	1985	1987	1992	1997
Comparison	150 (16.1) (929)	165 (18.1) (913)	131 (14.5) (903)	115 (12.7) (907)	138 (14.9) (929)
Background RH	40 (11.8) (340)	51 (15.3) (333)	60 (18.5) (325)	40 (12.2) (327)	44 (12.9) (340)
Low RH	29 (12.8) (226)	37 (16.8) (220)	35 (15.8) (222)	31 (14.2) (218)	31 (13.7) (226)
High RH	52 (22.4) (232)	39 (17.0) (229)	36 (15.9) (226)	36 (15.8) (228)	46 (19.8) (232)
Low plus High RH	81 (17.7) (458)	76 (16.9) (449)	71 (15.8) (448)	67 (15.0) (446)	77 (16.8) (458)

Table 13-69. Longitudinal Analysis of Cholesterol (Discrete) (Continued)

Dioxin Category	Normal in 1982: n in 1997	Normal in 1982: Number (%) High in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	779	80 (10.3)		
Background RH	300	26 (8.7)	0.75 (0.47,1.20)	0.236
Low RH	197	24 (12.2)	1.24 (0.76,2.02)	0.393
High RH	180	31 (17.2)	2.04 (1.29,3.24)	0.002
Low plus High RH	377	55 (14.6)	1.57 (1.08,2.29)	0.018

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal cholesterol level in 1982 (see Chapter 7, Statistical Methods).

The Model 2 longitudinal analysis revealed a marginally significant association between initial dioxin and high cholesterol levels in 1997 (Table 13-69(b): Adj. RR=1.23, p=0.072). The percentages of participants who had normal cholesterol levels in 1982 and high cholesterol levels in 1997 were 10.5, 15.9, and 17.9 in the low, medium, and high initial dioxin categories, respectively.

Model 3 analysis of the change in cholesterol values from normal in 1982 to high in 1997 revealed two significant contrasts: Ranch Hands in the high dioxin category versus Comparisons and Ranch Hands in the low and high dioxin categories combined versus Comparisons (Table 13-69(c): Adj. RR=2.04, p=0.002; Adj. RR=1.57, p=0.018, respectively). Of the Comparisons, 10.3 percent had normal cholesterol levels in 1982 and high cholesterol levels in 1997. Of the Ranch Hands, 17.2 percent in the high dioxin category and 14.6 percent in the low and high dioxin categories combined had normal cholesterol levels in 1982 and high cholesterol levels in 1997.

13.2.3.1.9 HDL Cholesterol (Continuous)

The longitudinal analyses in Models 1 through 3 did not reveal a significant association between dioxin and the change in mean HDL cholesterol levels (Table 13-70(a–c): p>0.10 for each analysis).

Table 13-70. Longitudinal Analysis of HDL Cholesterol (mg/dl) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS									
		Mean[a]/(n) Examination							
Occupational Category	Group	1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	*Ranch Hand*	*44.61 (798)*	*44.66 (781)*	*45.43 (772)*	*40.85 (763)*	*45.03 (798)*	*0.42*	*0.57*	*0.235*
	Comparison	*44.89 (955)*	*44.90 (937)*	*45.45 (928)*	*40.60 (926)*	*44.74 (955)*	*-0.15*		
Officer	Ranch Hand	45.96 (306)	46.24 (301)	46.94 (298)	42.59 (293)	46.91 (306)	0.95	0.28	0.844
	Comparison	46.31 (377)	46.43 (371)	47.05 (363)	41.90 (367)	46.98 (377)	0.67		
Enlisted Flyer	Ranch Hand	42.99 (145)	42.99 (142)	44.26 (140)	40.48 (138)	44.86 (145)	1.87	1.49	0.146
	Comparison	43.14 (142)	43.51 (141)	44.41 (140)	40.28 (136)	43.53 (142)	0.38		
Enlisted Groundcrew	Ranch Hand	44.13 (347)	44.00 (338)	44.61 (334)	39.52 (332)	43.50 (347)	-0.63	0.37	0.527
	Comparison	44.27 (436)	44.06 (425)	44.47 (425)	39.60 (423)	43.27 (436)	-1.00		

[a] Transformed from natural logarithm scale.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of natural logarithm of HDL cholesterol; results adjusted for natural logarithm of HDL cholesterol in 1982 and age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

Table 13-70. Longitudinal Analysis of HDL Cholesterol (mg/dl) (Continuous) (Continued)

(b) MODEL 2: RANCH HANDS – INITIAL DIOXIN							
Initial Dioxin Category Summary Statistics						Analysis Results for Log_2 (Initial Dioxin)[b]	
	Mean[a]/(n) Examination						
Initial Dioxin	1982	1985	1987	1992	1997	Adjusted Slope (Std. Error)	p-Value
Low	44.90 (149)	44.49 (145)	45.38 (148)	41.26 (144)	45.14 (149)	0.007 (0.008)	0.382
Medium	43.22 (154)	43.05 (152)	43.71 (150)	39.43 (148)	43.51 (154)		
High	42.38 (150)	42.38 (147)	43.37 (145)	38.86 (144)	43.39 (150)		

[a] Transformed from natural logarithm scale.
[b] Results based on difference between natural logarithm of 1997 HDL cholesterol and natural logarithm of 1982 HDL cholesterol versus $\log_2$ (initial dioxin); results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of 1982 HDL cholesterol, and age in 1997.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY								
	Mean[a]/(n) Examination							
Dioxin Category	1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
Comparison	44.90 (928)	44.80 (912)	45.37 (902)	40.54 (901)	44.65 (928)	–0.24		
Background RH	46.06 (339)	46.57 (332)	47.32 (324)	42.43 (322)	46.44 (339)	0.38	0.62	0.437
Low RH	44.89 (224)	44.77 (218)	45.54 (220)	41.52 (215)	45.07 (224)	0.18	0.42	0.598
High RH	42.15 (229)	41.91 (226)	42.81 (223)	38.26 (221)	42.97 (229)	0.83	1.07	0.105
Low plus High RH	43.48 (453)	43.29 (444)	44.14 (443)	39.83 (436)	44.00 (453)	0.52	0.76	0.161

[a] Transformed from natural logarithm scale.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of natural logarithm of 1997 HDL cholesterol; results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of 1982 HDL cholesterol, and age in 1997.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

13.2.3.1.10 HDL Cholesterol (Discrete)

Analyses of Models 1 through 3 showed no significant relations between dioxin and the percentage of participants with low HDL cholesterol values in 1997 (Table 13-71(a–c): p>0.19 for each analysis).

Table 13-71. Longitudinal Analysis of HDL Cholesterol (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) Low/(n) Examination 1982	1985	1987	1992	1997
All	***Ranch Hand***	***21 (2.6) (798)***	***30 (3.8) (781)***	***24 (3.1) (772)***	***82 (10.7) (763)***	***67 (8.4) (798)***
	Comparison	***20 (2.1) (955)***	***33 (3.5) (937)***	***22 (2.4) (928)***	***80 (8.6) (926)***	***74 (7.7) (955)***
Officer	Ranch Hand	9 (2.9) (306)	11 (3.7) (301)	7 (2.3) (298)	31 (10.6) (293)	16 (5.2) (306)
	Comparison	10 (2.7) (377)	13 (3.5) (371)	4 (1.1) (363)	28 (7.6) (367)	19 (5.0) (377)
Enlisted Flyer	Ranch Hand	4 (2.8) (145)	8 (5.6) (142)	8 (5.7) (140)	12 (8.7) (138)	16 (11.0) (145)
	Comparison	4 (2.8) (142)	8 (5.7) (141)	6 (4.3) (140)	14 (10.3) (136)	15 (10.6) (142)
Enlisted Groundcrew	Ranch Hand	8 (2.3) (347)	11 (3.3) (338)	9 (2.7) (334)	39 (11.7) (332)	35 (10.1) (347)
	Comparison	6 (1.4) (436)	12 (2.8) (425)	12 (2.8) (425)	38 (9.0) (423)	40 (9.2) (436)

Occupational Category	Group	Normal in 1982: n in 1997	Normal in 1982: Number (%) Low in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***777***	***57 (7.3)***	***1.06 (0.73,1.53)***	***0.760***
	Comparison	***935***	***65 (7.0)***		
Officer	Ranch Hand	297	13 (4.4)	0.94 (0.45,1.97)	0.872
	Comparison	367	17 (4.6)		
Enlisted Flyer	Ranch Hand	141	15 (10.6)	1.25 (0.56,2.78)	0.584
	Comparison	138	12 (8.7)		
Enlisted Groundcrew	Ranch Hand	339	29 (8.6)	1.03 (0.62,1.71)	0.920
	Comparison	430	36 (8.4)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal HDL cholesterol level in 1982 (see Chapter 7, Statistical Methods).

Table 13-71. Longitudinal Analysis of HDL Cholesterol (Discrete) (Continued)

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN

	Number (%) Low/(n) Examination				
Initial Dioxin	**1982**	**1985**	**1987**	**1992**	**1997**
Low	2 (1.3) (149)	5 (3.4) (145)	2 (1.4) (148)	13 (9.0) (144)	13 (8.7) (149)
Medium	4 (2.6) (154)	7 (4.6) (152)	4 (2.7) (150)	16 (10.8) (148)	15 (9.7) (154)
High	3 (2.0) (150)	7 (4.8) (147)	6 (4.1) (145)	16 (11.1) (144)	9 (6.0) (150)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1982			
Initial Dioxin	**n in 1997**	**Number (%) Low in 1997**	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**
Low	147	12 (8.2)	0.82 (0.60,1.12)	0.192
Medium	150	13 (8.7)		
High	147	7 (4.8)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal HDL cholesterol level in 1982 (see Chapter 7, Statistical Methods).

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY

	Number (%) Low/(n) Examination				
Dioxin Category	**1982**	**1985**	**1987**	**1992**	**1997**
Comparison	20 (2.2) (928)	33 (3.6) (912)	22 (2.4) (902)	78 (8.7) (901)	73 (7.9) (928)
Background RH	12 (3.5) (339)	11 (3.3) (332)	11 (3.4) (324)	34 (10.6) (322)	30 (8.8) (339)
Low RH	6 (2.7) (224)	10 (4.6) (218)	3 (1.4) (220)	19 (8.8) (215)	19 (8.5) (224)
High RH	3 (1.3) (229)	9 (4.0) (226)	9 (4.0) (223)	26 (11.8) (221)	18 (7.9) (229)
Low plus High RH	9 (2.0) (453)	19 (4.3) (444)	12 (2.7) (443)	45 (10.3) (436)	37 (8.2) (453)

Table 13-71. Longitudinal Analysis of HDL Cholesterol (Discrete) (Continued)

Dioxin Category	Normal in 1982: n in 1997	Normal in 1982: Number (%) Low in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	908	64 (7.0)		
Background RH	327	25 (7.6)	1.25 (0.77,2.03)	0.374
Low RH	218	16 (7.3)	1.03 (0.58,1.83)	0.926
High RH	226	16 (7.1)	0.85 (0.47,1.52)	0.581
Low plus High RH	444	32 (7.2)	0.93 (0.60,1.46)	0.759

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal HDL cholesterol level in 1982 (see Chapter 7, Statistical Methods).

13.2.3.1.11 Cholesterol-HDL Ratio (Continuous)

The Models 1 through 3 analyses did not reveal a significant association between the cholesterol-HDL ratio and dioxin (Table 13-72(a–c): $p>0.23$ for each analysis).

Table 13-72. Longitudinal Analysis of Cholesterol-HDL Ratio (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Mean[a]/(n) Examination 1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	*Ranch Hand*	*4.71 (798)*	*4.77 (781)*	*4.71 (772)*	*5.23 (763)*	*4.65 (798)*	*-0.06*	*-0.01*	*0.519*
	Comparison	*4.77 (955)*	*4.80 (937)*	*4.71 (928)*	*5.27 (926)*	*4.71 (955)*	*-0.05*		
Officer	Ranch Hand	4.58 (306)	4.62 (301)	4.56 (298)	4.99 (293)	4.36 (306)	-0.22	-0.10	0.237
	Comparison	4.57 (377)	4.60 (371)	4.53 (363)	5.04 (367)	4.45 (377)	-0.12		
Enlisted Flyer	Ranch Hand	5.00 (145)	5.06 (142)	4.88 (140)	5.32 (138)	4.72 (145)	-0.28	-0.06	0.255
	Comparison	5.16 (142)	5.06 (141)	4.95 (140)	5.45 (136)	4.94 (142)	-0.22		
Enlisted Groundcrew	Ranch Hand	4.71 (347)	4.79 (338)	4.78 (334)	5.42 (332)	4.89 (347)	0.18	0.12	0.400
	Comparison	4.81 (436)	4.89 (425)	4.79 (425)	5.43 (423)	4.87 (436)	0.06		

[a] Transformed from natural logarithm scale.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of natural logarithm of cholesterol-HDL ratio; results adjusted for natural logarithm of cholesterol-HDL ratio in 1982 and age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

Table 13-72. Longitudinal Analysis of Cholesterol-HDL Ratio (Continuous) (Continued)

(b) MODEL 2: RANCH HANDS – INITIAL DIOXIN							
Initial Dioxin Category Summary Statistics						Analysis Results for Log_2 (Initial Dioxin)[b]	
	Mean[a]/(n) Examination						
Initial Dioxin	1982	1985	1987	1992	1997	Adjusted Slope (Std. Error)	p-Value
Low	4.70 (149)	4.81 (145)	4.73 (148)	5.17 (144)	4.51 (149)	0.005 (0.008)	0.589
Medium	4.85 (154)	4.98 (152)	4.93 (150)	5.43 (148)	4.88 (154)		
High	5.10 (150)	5.12 (147)	5.02 (145)	5.59 (144)	4.98 (150)		

[a] Transformed from natural logarithm scale.

[b] Results based on difference between natural logarithm of 1997 cholesterol-HDL ratio and natural logarithm of 1982 GGT versus log_2 (initial dioxin); results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of 1982 cholesterol-HDL ratio, and age in 1997.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY								
	Mean[a]/(n) Examination							
Dioxin Category	1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
Comparison	4.76 (928)	4.81 (912)	4.71 (902)	5.28 (901)	4.72 (928)	–0.04		
Background RH	4.50 (339)	4.52 (332)	4.48 (324)	4.99 (322)	4.47 (339)	–0.03	0.01	0.473
Low RH	4.69 (224)	4.77 (218)	4.69 (220)	5.16 (215)	4.57 (224)	–0.12	–0.08	0.281
High RH	5.08 (229)	5.17 (226)	5.10 (223)	5.64 (221)	5.01 (229)	–0.06	–0.02	0.971
Low plus High RH	4.88 (453)	4.97 (444)	4.89 (443)	5.40 (436)	4.79 (453)	–0.09	–0.05	0.505

[a] Transformed from natural logarithm scale.

[b] Difference between 1997 and 1982 examination means after transformation to original scale.

[c] P-value is based on analysis of natural logarithm of 1997 cholesterol-HDL ratio; results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of 1982 cholesterol-HDL ratio, and age in 1997.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

13.2.3.1.12 Cholesterol-HDL Ratio (Discrete)

The longitudinal analyses in Models 1 through 3 did not reveal a significant association between dioxin and the percentage of participants who had a normal cholesterol-HDL ratio in 1982 and a high cholesterol-HDL ratio in 1997 (Table 13-73(a–c): p>0.10 for each analysis).

Table 13-73. Longitudinal Analysis of Cholesterol-HDL Ratio (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) High/(n) Examination 1982	1985	1987	1992	1997
All	***Ranch Hand***	***350 (43.9) (798)***	***352 (45.1) (781)***	***335 (43.4) (772)***	***432 (56.6) (763)***	***324 (40.6) (798)***
	Comparison	***423 (44.3) (955)***	***415 (44.3) (937)***	***401 (43.2) (928)***	***533 (57.6) (926)***	***404 (42.3) (955)***
Officer	Ranch Hand	120 (39.2) (306)	132 (43.9) (301)	124 (41.6) (298)	144 (49.1) (293)	99 (32.4) (306)
	Comparison	151 (40.1) (377)	140 (37.7) (371)	134 (36.9) (363)	182 (49.6) (367)	117 (31.0) (377)
Enlisted Flyer	Ranch Hand	74 (51.0) (145)	69 (48.6) (142)	61 (43.6) (140)	83 (60.1) (138)	56 (38.6) (145)
	Comparison	77 (54.2) (142)	71 (50.4) (141)	76 (54.3) (140)	84 (61.8) (136)	71 (50.0) (142)
Enlisted Groundcrew	Ranch Hand	156 (45.0) (347)	151 (44.7) (338)	150 (44.9) (334)	205 (61.7) (332)	169 (48.7) (347)
	Comparison	195 (44.7) (436)	204 (48.0) (425)	191 (44.9) (425)	267 (63.1) (423)	216 (49.5) (436)

Occupational Category	Group	Normal in 1982: n in 1997	Number (%) High in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***448***	***90 (20.1)***	***0.82 (0.60,1.12)***	***0.206***
	Comparison	***532***	***125 (23.5)***		
Officer	Ranch Hand	186	27 (14.5)	1.00 (0.58,1.74)	0.996
	Comparison	226	33 (14.6)		
Enlisted Flyer	Ranch Hand	71	16 (22.5)	0.81 (0.37,1.78)	0.598
	Comparison	65	17 (26.2)		
Enlisted Groundcrew	Ranch Hand	191	47 (24.6)	0.72 (0.47,1.10)	0.131
	Comparison	241	75 (31.1)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal cholesterol-HDL ratio in 1982 (see Chapter 7, Statistical Methods).

Table 13-73. Longitudinal Analysis of Cholesterol-HDL Ratio (Discrete) (Continued)

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN

Initial Dioxin	Number (%) High/(n) Examination 1982	1985	1987	1992	1997
Low	61 (40.9) (149)	66 (45.5) (145)	65 (43.9) (148)	79 (54.9) (144)	51 (34.2) (149)
Medium	74 (48.1) (154)	75 (49.3) (152)	73 (48.7) (150)	97 (65.5) (148)	72 (46.8) (154)
High	82 (54.7) (150)	78 (53.1) (147)	74 (51.0) (145)	92 (63.9) (144)	78 (52.0) (150)

Initial Dioxin Category Summary Statistics: Initial Dioxin	Normal in 1982: n in 1997	Number (%) High in 1997	Analysis Results for Log_2 (Initial Dioxin)[a]: Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	88	15 (17.0)	1.15 (0.89,1.48)	0.278
Medium	80	21 (26.3)		
High	68	17 (25.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal cholesterol-HDL ratio in 1982 (see Chapter 7, Statistical Methods).

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY

Dioxin Category	Number (%) High/(n) Examination 1982	1985	1987	1992	1997
Comparison	407 (43.9) (928)	406 (44.5) (912)	391 (43.3) (902)	518 (57.5) (901)	395 (42.6) (928)
Background RH	131 (38.6) (339)	130 (39.2) (332)	120 (37.0) (324)	160 (49.7) (322)	119 (35.1) (339)
Low RH	91 (40.6) (224)	93 (42.7) (218)	94 (42.7) (220)	120 (55.8) (215)	80 (35.7) (224)
High RH	126 (55.0) (229)	126 (55.8) (226)	118 (52.9) (223)	148 (67.0) (221)	121 (52.8) (229)
Low plus High RH	217 (47.9) (453)	219 (49.3) (444)	212 (47.9) (443)	268 (61.5) (436)	201 (44.4) (453)

Table 13-73. Longitudinal Analysis of Cholesterol-HDL Ratio (Discrete) (Continued)

Dioxin Category	Normal in 1982: n in 1997	Normal in 1982: Number (%) High in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	521	124 (23.8)		
Background RH	208	35 (16.8)	0.70 (0.46 ,1.07)	0.102
Low RH	133	25 (18.8)	0.74 (0.45,1.20)	0.216
High RH	103	28 (27.2)	1.03 (0.63,1.68)	0.899
Low plus High RH	236	53 (22.5)	0.85 (0.59,1.24)	0.408

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal cholesterol-HDL ratio in 1982 (see Chapter 7, Statistical Methods).

13.2.3.1.13 Triglycerides (Continuous)

The Model 1 analysis of the change in triglyceride levels did not uncover a significant difference between overall Ranch Hands and Comparisons or within each occupational stratum (Table 13-74(a): p>0.12 for each contrast). The Model 2 analysis did not reveal a significant association between the change in triglyceride levels and initial dioxin (Table 13-74(b): p=0.751).

Model 3 analysis of the change in mean triglyceride levels between 1982 and 1997 revealed two significant contrasts: Ranch Hands in the high dioxin category versus Comparisons and Ranch Hands in the low and high dioxin categories combined versus Comparisons (Table 13-74(c): difference of examination mean change=11.8 mg/dl, p=0.020; difference of examination mean change=5.4 mg/dl, p=0.094, respectively). The examination mean changes for Ranch Hands in the high dioxin category, Ranch Hands in the low and high dioxin categories combined, and Comparisons were 13.1 mg/dl, 6.7 mg/dl, and 1.3 mg/dl, respectively.

Table 13-74. Longitudinal Analysis of Triglycerides (mg/dl) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Mean[a]/(n) Examination 1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	***Ranch Hand***	***118.8 (803)***	***117.1 (786)***	***120.2 (777)***	***146.6 (777)***	***122.7 (803)***	***4.0***	***3.2***	***0.478***
	Comparison	***120.9 (956)***	***119.1 (938)***	***119.4 (929)***	***146.1 (933)***	***121.8 (956)***	***0.8***		
Officer	Ranch Hand	118.8 (308)	116.3 (303)	115.1 (300)	143.1 (299)	113.7 (308)	–5.1	–1.0	0.780
	Comparison	115.5 (377)	111.9 (371)	111.8 (363)	137.7 (370)	111.4 (377)	–4.1		
Enlisted Flyer	Ranch Hand	129.1 (146)	122.7 (143)	126.7 (141)	145.0 (143)	125.0 (146)	–4.1	–8.5	0.177
	Comparison	134.2 (142)	130.4 (141)	130.0 (140)	157.3 (138)	138.6 (142)	4.4		
Enlisted Groundcrew	Ranch Hand	114.6 (349)	115.5 (340)	122.3 (336)	150.4 (335)	130.3 (349)	15.7	11.3	0.128
	Comparison	121.6 (437)	122.1 (426)	122.8 (426)	150.0 (425)	126.1 (437)	4.4		

[a] Transformed from natural logarithm scale.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of natural logarithm of triglycerides; results adjusted for natural logarithm of triglycerides in 1982 and age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

Table 13-74. Longitudinal Analysis of Triglycerides (mg/dl) (Continuous) (Continued)

(b) MODEL 2: RANCH HANDS – INITIAL DIOXIN							
Initial Dioxin Category Summary Statistics						Analysis Results for Log_2 (Initial Dioxin)[b]	
	Mean[a]/(n) Examination						
Initial Dioxin	1982	1985	1987	1992	1997	Adjusted Slope (Std. Error)	p-Value
Low	122.1 (151)	120.8 (147)	120.1 (150)	143.2 (146)	117.6 (151)	0.006 (0.020)	0.751
Medium	129.2 (156)	129.1 (154)	142.9 (152)	163.3 (152)	141.4 (156)		
High	129.5 (151)	133.2 (148)	133.6 (146)	161.1 (148)	143.0 (151)		

[a] Transformed from natural logarithm scale.

[b] Results based on difference between natural logarithm of 1997 triglycerides and natural logarithm of 1982 triglycerides versus $\log_2$ (initial dioxin); results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of 1982 triglycerides and age in 1997.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY								
	Mean[a]/(n) Examination							
Dioxin Category	1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
Comparison	120.1 (929)	118.7 (913)	118.7 (903)	145.4 (907)	121.4 (929)	1.3		
Background RH	107.7 (339)	103.7 (332)	105.5 (324)	134.4 (326)	108.6 (339)	0.8	–0.5	0.377
Low RH	119.8 (226)	120.4 (220)	120.5 (222)	144.0 (218)	120.8 (226)	1.0	–0.3	0.820
High RH	134.3 (232)	135.0 (229)	144.1 (226)	167.8 (228)	147.3 (232)	13.1	11.8	0.020
Low plus High RH	126.9 (458)	127.6 (449)	131.9 (448)	155.7 (446)	133.6 (458)	6.7	5.4	0.094

[a] Transformed from natural logarithm scale.

[b] Difference between 1997 and 1982 examination means after transformation to original scale.

[c] P-value is based on analysis of natural logarithm of 1997 triglycerides; results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of 1982 triglycerides, and age in 1997.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

13.2.3.1.14 Triglycerides (Discrete)

The Model 1 analysis of the percentage of participants with a normal triglyceride level in 1982 and a high triglyceride level in 1997 did not show a significant difference between overall Ranch Hands and Comparisons or within each occupational stratum (Table 13-75(a): p>0.12 for each contrast).

Table 13-75. Longitudinal Analysis of Triglycerides (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) High/(n) Examination 1982	1985	1987	1992	1997
All	***Ranch Hand***	***248 (30.9) (803)***	***58 (7.4) (786)***	***59 (7.6) (777)***	***88 (11.3) (777)***	***179 (22.3) (803)***
	Comparison	***313 (32.7) (956)***	***61 (6.5) (938)***	***60 (6.5) (929)***	***84 (9.0) (933)***	***203 (21.2) (956)***
Officer	Ranch Hand	84 (27.3) (308)	30 (9.9) (303)	21 (7.0) (300)	33 (11.0) (299)	53 (17.2) (308)
	Comparison	113 (30.0) (377)	24 (6.5) (371)	25 (6.9) (363)	32 (8.6) (370)	62 (16.4) (377)
Enlisted Flyer	Ranch Hand	55 (37.7) (146)	14 (9.8) (143)	12 (8.5) (141)	20 (14.0) (143)	30 (20.5) (146)
	Comparison	52 (36.6) (142)	10 (7.1) (141)	9 (6.4) (140)	11 (8.0) (138)	42 (29.6) (142)
Enlisted Groundcrew	Ranch Hand	109 (31.2) (349)	14 (4.1) (340)	26 (7.7) (336)	35 (10.4) (335)	96 (27.5) (349)
	Comparison	148 (33.9) (437)	27 (6.3) (426)	26 (6.1) (426)	41 (9.6) (425)	99 (22.7) (437)

Occupational Category	Group	Normal in 1982: n in 1997	Number (%) High in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***555***	***66 (11.9)***	***1.31 (0.90,1.89)***	***0.159***
	Comparison	***643***	***60 (9.3)***		
Officer	Ranch Hand	224	20 (8.9)	1.44 (0.73,2.82)	0.291
	Comparison	264	17 (6.4)		
Enlisted Flyer	Ranch Hand	91	8 (8.8)	0.69 (0.26,1.80)	0.443
	Comparison	90	11 (12.2)		
Enlisted Groundcrew	Ranch Hand	240	38 (15.8)	1.48 (0.89,2.46)	0.127
	Comparison	289	32 (11.1)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal triglyceride level in 1982 (see Chapter 7, Statistical Methods).

Table 13-75. Longitudinal Analysis of Triglycerides (Discrete) (Continued)

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN					
	Number (%) High/(n) Examination				
Initial Dioxin	1982	1985	1987	1992	1997
Low	49 (32.5) (151)	13 (8.8) (147)	9 (6.0) (150)	14 (9.6) (146)	36 (23.8) (151)
Medium	56 (35.9) (156)	16 (10.4) (154)	16 (10.5) (152)	25 (16.4) (152)	44 (28.2) (156)
High	56 (37.1) (151)	11 (7.4) (148)	18 (12.3) (146)	19 (12.8) (148)	49 (32.5) (151)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1982			
Initial Dioxin	n in 1997	Number (%) High in 1997	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	102	14 (13.7)	1.07 (0.83,1.38)	0.608
Medium	100	12 (12.0)		
High	95	19 (20.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal triglyceride level in 1982 (see Chapter 7, Statistical Methods).

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY					
	Number (%) High/(n) Examination				
Dioxin Category	1982	1985	1987	1992	1997
Comparison	300 (32.3) (929)	58 (6.4) (913)	57 (6.3) (903)	80 (8.8) (907)	195 (21.0) (929)
Background RH	83 (24.5) (339)	17 (5.1) (332)	16 (4.9) (324)	30 (9.2) (326)	46 (13.6) (339)
Low RH	75 (33.2) (226)	20 (9.1) (220)	14 (6.3) (222)	21 (9.6) (218)	52 (23.0) (226)
High RH	86 (37.1) (232)	20 (8.7) (229)	29 (12.8) (226)	37 (16.2) (228)	77 (33.2) (232)
Low plus High RH	161 (35.2) (458)	40 (8.9) (449)	43 (9.6) (448)	58 (13.0) (446)	129 (28.2) (458)

Table 13-75. Longitudinal Analysis of Triglycerides (Discrete) (Continued)

	Normal in 1982			
Dioxin Category	n in 1997	Number (%) High in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	629	58 (9.2)		
Background RH	256	19 (7.4)	0.88 (0.51,1.52)	0.649
Low RH	151	17 (11.3)	1.29 (0.72,2.30)	0.390
High RH	146	28 (19.2)	1.97 (1.19,3.26)	0.008
Low plus High RH	297	45 (15.2)	1.59 (1.04,2.44)	0.034

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal triglyceride level in 1982 (see Chapter 7, Statistical Methods).

The Model 2 analysis did not reveal a significant association between the change in triglyceride levels and initial dioxin (Table 13-75(b): p=0.608). Model 3 analysis of the change in triglyceride values from normal in 1982 to high in 1997 revealed two significant contrasts: Ranch Hands in the high dioxin category versus Comparisons and Ranch Hands in the low and high dioxin categories combined versus Comparisons (Table 13-75(c): Adj. RR=1.97, p=0.008; Adj. RR=1.59, p=0.034, respectively). Of the Comparisons, 9.2 percent had normal triglyceride levels in 1982 and high triglyceride levels in 1997. Of the Ranch Hands, 19.2 percent in the high dioxin category and 15.2 percent in the low and high dioxin categories combined had normal triglyceride levels in 1982 and high triglyceride levels in 1997.

13.3 DISCUSSION

The historical, physical examination, and laboratory parameters included in the gastrointestinal assessment are well established in clinical practice as screening tools in the outpatient investigation of digestive disorders. In the diagnosis of digestive disorders, it is important to recognize the limitations of the history and physical examination. Rather than pointing to a particular diagnosis, digestive symptoms are frequently nonspecific and intermittent. In this setting, even the best-designed medical history questionnaire can be subject to error. "Ulcer" and "colitis" are diagnoses that are commonly reported but often not accurately established. As a common target organ for situational stress, the bowel frequently gives rise to symptoms that can be severe but that are functional in nature and resolve over time. These caveats highlight the importance of the type of medical record verification conducted in the current study.

The physical examination of the gastrointestinal system is often of limited value and can be misleading in the differential diagnosis. For example, the detection of enlargement of the liver in the obese patient is unreliable. In obstructive airway disease, with hyperinflation of the lungs and flattening of the

diaphragms, the liver edge may descend abnormally below the right costal margin in the absence of hepatomegaly. The span of the liver by palpation or percussion is often an unreliable index of liver size.

Data collected in the laboratory can provide early insight into the presence of occult liver disease despite the limitations in the history and physical examination. The four hepatic enzymes analyzed as dependent variables (AST, ALT, GGT, and LDH) are commonly ordered in the outpatient setting. These enzymes, of which GGT is the most sensitive, are present in high intracellular concentration. They also are elevated in fatty infiltration of the liver associated with obesity and in virtually all toxic, inflammatory, and neoplastic diseases with hepatic involvement.

The hepatic enzymes are used in the detection and follow-up of parenchymal liver disease. The serum alkaline phosphatase and bilirubin are reflective of hepatobiliary function and are elevated in "cholestatic" or "obstructive" diseases. Although present in virtually all organ systems, the serum alkaline phosphatase in the adult population under study is of dual origin and close to a even mixture of liver- and bone-derived fractions. An elevated alkaline phosphatase is not diagnostic of liver disease and may occur in a broad range of unrelated clinical conditions including drug-induced cholestasis, Paget's disease (3% of males over age 40), neoplasia with metastases to bone, and congestive heart failure.

Similarly, the bilirubin measurements are subject to numerous hereditary and acquired disorders unrelated to intrinsic hepatic disease. The benign hyperbilirubinemia of Gilbert's syndrome will occur in 5 percent of the population under study. Many medications, including over-the-counter preparations, have been implicated in the overproduction of bilirubin that occurs in the hemolytic reactions associated with glucose-6-phosphate dehydrogenase deficiency that may be present in up to 15 percent of Black American males.

In this follow-up examination, with two exceptions, none of the analyses of historical (verified medical records review) or physical examination variables revealed any significant group differences or evidence for liver disease associated with the 1987 body burden of dioxin. Consistent with the 1992 examinations, Ranch Hands were significantly less likely than Comparisons to have a history of jaundice (1.4% vs. 2.9%), a finding that is consistent with the highly significant ($p<0.001$) inverse dose-response pattern in the model relating this variable to 1987 serum dioxin. Also consistent with the 1992 follow-up examination, Ranch Hands were more likely than Comparisons to have a history of other liver disorders, primarily based on enlisted groundcrew (30.8% vs. 25.2%). An increasing history of other liver disorders as dioxin levels increased also was observed. Twelve percent of this category of "other liver disorders" comprised participants with nonspecific laboratory test elevations at previous examinations.

The laboratory data examined can be divided broadly into parenchymal (serum enzymes), hepatobiliary (serum bilirubin and alkaline phosphatase), lipid or carbohydrate indices, and a 10-element protein profile including prealbumin, albumin, α-1-acid glycoprotein, α-1-antitrypsin, α-2-macroglobulin, apolipoprotein B, C3 complement, C4 complement, haptoglobin, and transferrin. The components of the protein profile were selected to provide a comprehensive reflection of multiple organ systems involved in homeostasis and to investigate the possibility of a subclinical inflammatory process that might be associated with prior TCDD exposure or the current body burden of dioxin. Produced in the liver, the proteins measured are most sensitive to hepatic function but also provide a reliable assessment of nutritional status. Selected proteins (α-1-acid glycoprotein, α-1-antitrypsin, and haptoglobin) are nonspecifically elevated in association with inflammation, whereas reductions in the C3 and C4 complement indices are associated with immune system responses.

Few of the laboratory analyses revealed any significant differences between the Ranch Hand and Comparison cohorts. Ranch Hands continued to have a slightly higher mean alkaline phosphatase than

Comparisons by continuous analysis. In the analyses relating alkaline phosphatase to the initial and the 1987 body burden of dioxin within Ranch Hands, a marginally significant inverse relation was noted. In the analyses of laboratory data in discrete form, no significant group differences were defined.

The analyses of two protein variables in continuous form, α-1-antitrypsin and haptoglobin, yielded statistically significant (p=0.002 for both variables) overall group differences with Ranch Hands adversely affected. In neither instance was there any evidence for an association with 1987 serum dioxin levels and, by all discrete analyses, the prevalence of abnormalities was similar in each cohort.

Several analyses yielded results that have been documented consistently in prior examinations. Although no overall group differences were defined by both continuous and discrete analyses, three of four liver enzymes—ALT, AST, and GGT—revealed significant positive associations with 1987 serum dioxin levels. Similar results were noted as well in the analysis of serum triglycerides. These results, while consistent with a dose-response effect, might be explained as well on the basis of the hyperlipidemia and fatty infiltration of the liver that occur in association with obesity. A causal relation with prior dioxin exposure remains to be established.

Dependent variable-covariate associations yielded results similar to those documented in previous examinations and that are well established in clinical practice. Highly significant positive correlations were noted relating lifetime alcohol consumption with the history of chronic liver disease and cirrhosis, the finding of enlargement of the liver upon physical examination, and an elevation in GGT, the most sensitive liver enzyme. The mean creatine phosphokinase level in Blacks was almost twice as high as in non-Blacks, a finding that was noted in both the 1987 and 1992 examinations and that appears to be race- and gender-specific.

Throughout 15 years of observation, the longitudinal analyses have yielded marginally significant results in several of the laboratory indices, most of which were similar to those documented in the 1992 examination. Although no significant overall group differences were identified, a consistent gradual reduction in serum AST occurred in both Ranch Hands and Comparisons across all occupational and exposure categories. In the analyses of ALT in discrete form, Ranch Hand enlisted groundcrew, those most heavily exposed to dioxin, remained less likely than Comparisons to have abnormal elevations in this index (5.6% vs. 7.9%, respectively) in 1997. Relative to Comparisons, the increase in mean serum triglyceride levels over time was most pronounced in Ranch Hands in the highest serum dioxin category in a pattern consistent with a dose-response effect (13.1 mg vs. 1.3 mg; p=0.020). Finally, Ranch Hands in the enlisted groundcrew occupational stratum whose cholesterol levels were normal in 1982 were significantly more likely than Comparisons to develop abnormal elevations in 1997 (15.6% vs. 9.9%), an effect most pronounced in those participants with the highest levels of serum dioxin relative to Comparisons (17.2% vs. 10.3%).

Data analyzed for the gastrointestinal assessment confirm observations that would be anticipated in clinical practice and reflect no apparent increase in organ-specific morbidity in Ranch Hands relative to Comparisons. Although the results cited above are consistent with a subtle effect of dioxin on lipid metabolism, an association with body habitus and obesity cannot be excluded.

13.4 SUMMARY

13.4.1 Model 1: Group Analysis

The adjusted group analysis for medical records variables revealed a significant difference between Ranch Hands and Comparisons over all occupational strata for jaundice. Comparisons had a greater history of jaundice than Ranch Hands.

The adjusted Model 1 analyses of the continuous variables found that Ranch Hands had significantly higher mean levels of alkaline phosphatase, α-1-antitrypsin, haptoglobin, and transferrin than Comparisons. In the discrete analyses, significantly more Ranch Hands than Comparisons had high haptoglobin levels and more Comparisons than Ranch Hands had evidence of prior hepatitis B infection and low transferrin values.

After stratifying by occupation, the adjusted analyses revealed significantly lower mean levels of serum amylase, apolipoprotein B, and C4 complement among the Ranch Hand officers versus Comparison officers. In the discrete analysis, more Comparison officers than Ranch Hand officers had prior hepatitis B infection. Ranch Hand enlisted flyers had a significantly lower percentage of high apolipoprotein B values than Comparison enlisted flyers.

The adjusted analysis of the continuous variables showed that among the enlisted groundcrew, the Ranch Hand mean levels of alkaline phosphatase, α-1-acid glycoprotein, α-1-antitrypsin, and haptoglobin were significantly higher than the corresponding Comparison group mean levels. The adjusted discrete analyses found significantly more high triglyceride levels and low prealbumin levels among enlisted groundcrew Ranch Hands than among enlisted groundcrew Comparisons. A significantly smaller prevalence of serological evidence of prior hepatitis B infection was seen for Ranch Hand enlisted groundcrew versus Comparison enlisted groundcrew.

The results of all unadjusted and adjusted Model 1 analyses are summarized in Table 13-76.

Table 13-76. Summary of Group Analysis (Model 1) for Gastrointestinal Variables (Ranch Hands vs. Comparisons)

	UNADJUSTED			
Variable	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Medical Records				
Uncharacterized Hepatitis (D)	NS	NS	NS	NS
Jaundice (Unspecified) (D)	−0.025	ns*	NS	ns*
Chronic Liver Disease and Cirrhosis (Alcohol-related) (D)	NS	NS	ns	ns
Chronic Liver Disease and Cirrhosis (Non-alcohol-related) (D)	NS	NS	ns	NS
Liver Abscess and Sequelae of Chronic Liver Disease (D)	NS	ns	--	NS
Enlarged Liver (Hepatomegaly) (D)	ns	ns	NS	ns*
Other Liver Disorders (D)	NS*	NS	NS	NS*
Physical Examination				
Current Hepatomegaly (D)	NS	NS	NS	NS

Table 13-76. Summary of Group Analysis (Model 1) for Gastrointestinal Variables (Ranch Hands vs. Comparisons) (Continued)

	UNADJUSTED			
Variable	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Laboratory				
AST (C)	NS	NS	ns	NS
AST (D)	NS	NS	ns	NS
ALT (C)	NS	NS	ns	NS
ALT (D)	NS	NS	ns	ns
GGT (C)	NS	NS	ns	NS
GGT (D)	NS	NS	NS	ns
Alkaline Phosphatase (C)	+0.024	NS	NS	+0.030
Alkaline Phosphatase (D)	NS	ns	NS	NS*
Total Bilirubin (C)	ns	NS	ns	NS
Total Bilirubin (D)	ns	ns	NS	ns
Direct Bilirubin (D)	ns	ns	--	ns
Lactic Dehydrogenase (C)	NS	ns	ns	NS
Lactic Dehydrogenase (D)	ns	ns	NS	ns
Cholesterol (C)	ns	ns	ns	NS
Cholesterol (D)	NS	ns	ns	NS
HDL Cholesterol (C)[a]	NS	ns	NS	ns
HDL Cholesterol (D)	NS	NS	NS	NS
Cholesterol-HDL Ratio (C)	ns	ns	ns	NS
Cholesterol-HDL Ratio (D)	NS	NS	ns	NS
Triglycerides (C)	NS	NS	ns	NS
Triglycerides (D)	NS	NS	ns	NS*
Creatine Phosphokinase (C)	NS	NS	ns	NS
Creatine Phosphokinase (D)	ns	ns	ns	NS
Serum Amylase (C)	NS	−0.048	NS	NS
Serum Amylase (D)	ns	ns*	NS	NS
Antibodies for Hepatitis A (D)	ns	NS	NS	ns
Serological Evidence of Prior Hepatitis B Infection (D)	−0.001	−0.031	ns*	−0.036
Current Hepatitis B (D)	ns	--	--	ns
Antibodies for Hepatitis C (D)	ns	ns	ns	ns
Antibodies for Hepatitis D (D)	--	--	--	--
Stool Hemoccult (D)	ns	ns	ns	ns
Prealbumin (C)[a]	ns	ns	NS	ns
Prealbumin (D)	NS	NS	NS	NS*
Albumin (C)[a]	ns	ns	NS	NS
Albumin (D)	ns	NS	ns	ns
α-1-Acid Glycoprotein (C)	NS	ns	ns	+0.044
α-1-Acid Glycoprotein (D)	NS	ns	NS	NS
α-1-Antitrypsin (C):	+0.002	NS	NS	+0.001
α-1-Antitrypsin (D):				
Low vs. Normal	ns	NS	NS	ns
High vs. Normal	NS	NS	ns	NS
α-2-Macroglobulin (C)	ns	ns	ns	ns
α-2-Macroglobulin (D)	ns	ns	ns	ns
Apolipoprotein B (C)	ns	ns*	ns	NS
Apolipoprotein B (D)	ns*	ns	−0.007	NS
C3 Complement (C)[a]	NS	NS	ns	NS
C3 Complement (D)	ns	ns	ns	NS

Table 13-76. Summary of Group Analysis (Model 1) for Gastrointestinal Variables (Ranch Hands vs. Comparisons) (Continued)

Variable	UNADJUSTED All	Officer	Enlisted Flyer	Enlisted Groundcrew
C4 Complement (C)[a]	ns	−0.024	NS*	ns
C4 Complement (D)	NS	NS	ns	--
Haptoglobin (C)	+0.002	NS	NS	+0.016
Haptoglobin (D)	+0.017	NS	NS	NS*
Transferrin (C)[a]	+0.044	NS	NS	NS*
Transferrin (D)	−0.036	ns*	ns	ns

Note: NS or ns: Not significant (p>0.10).
NS* or ns*: Marginally significant (0.05<p≤0.10).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00 for discrete analysis; difference of means nonnegative for continuous analysis.
−: Relative risk <1.00 for discrete analysis; difference of means negative for continuous analysis.
--: Analysis not performed because of the sparse number of participants with an abnormality.
[a] Negative difference considered adverse for this variable.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analyses or difference of means negative for continuous analysis.

Variable	ADJUSTED All	Officer	Enlisted Flyer	Enlisted Groundcrew
Medical Records				
Uncharacterized Hepatitis (D)	NS	NS	NS	NS
Jaundice (Unspecified) (D)	−0.028	ns	NS	ns*
Chronic Liver Disease and Cirrhosis (Alcohol-related) (D)	ns	NS	ns	ns
Chronic Liver Disease and Cirrhosis (Non-alcohol-related) (D)	NS	NS	ns	NS
Liver Abscess and Sequelae of Chronic Liver Disease (D)	NS	--	--	--
Enlarged Liver (Hepatomegaly) (D)	ns	ns	NS	ns*
Other Liver Disorders (D)	NS*	NS	ns	NS*
Physical Examination				
Current Hepatomegaly (D)	NS	NS	--	NS
Laboratory				
AST (C)	NS	NS	ns	NS
AST (D)	NS	NS	ns	NS
ALT (C)	NS	NS	ns	NS
ALT (D)	NS	NS	ns	ns
GGT (C)	NS	NS	NS	NS
GGT (D)	NS	NS	NS	ns
Alkaline Phosphatase (C)	+0.016	NS	NS	+0.021
Alkaline Phosphatase (D)	NS	ns	NS	NS*
Total Bilirubin (C)	NS	NS	ns	NS
Total Bilirubin (D)	ns	ns	NS	ns
Direct Bilirubin (D)	ns	ns	--	--

Table 13-76. Summary of Group Analysis (Model 1) for Gastrointestinal Variables (Ranch Hands vs. Comparisons) (Continued)

Variable	ADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Lactic Dehydrogenase (C)	NS	ns	ns	NS
Lactic Dehydrogenase (D)	ns	ns	NS	ns
Cholesterol (C)	ns	ns	ns	NS
Cholesterol (D)	NS	ns	NS	NS
HDL Cholesterol (C)[a]	NS	ns	NS*	ns
HDL Cholesterol (D)	NS	NS	ns	NS
Cholesterol-HDL Ratio (C)	ns	ns	ns*	NS
Cholesterol-HDL Ratio (D)	NS	NS	ns*	NS
Triglycerides (C)	NS	NS	ns	NS
Triglycerides (D)	NS	NS	ns	+0.047
Creatine Phosphokinase (C)	NS	NS	ns	NS
Creatine Phosphokinase (D)	ns	ns	ns	NS
Serum Amylase (C)	ns	–0.037	NS	NS
Serum Amylase (D)	ns	ns*	NS	NS
Antibodies for Hepatitis A (D)	ns	ns	NS	ns
Serological Evidence of Prior Hepatitis B Infection (D)	–<0.001	–0.024	ns*	–0.035
Current Hepatitis B (D)	ns	--	--	ns
Antibodies for Hepatitis C (D)	ns	ns	ns	ns
Antibodies for Hepatitis D (D)	--	--	--	--
Stool Hemoccult (D)	ns	ns	ns	ns
Prealbumin (C)[a]	ns	ns	NS	ns
Prealbumin (D)	NS	NS	NS	+0.043
Albumin (C)[a]	ns	ns	NS	NS
Albumin (D)	ns	NS	--	--
α-1-Acid Glycoprotein (C)	NS	ns	NS	+0.030
α-1-Acid Glycoprotein (D)	NS	ns	NS	NS*
α-1-Antitrypsin (C)	+0.001	NS	NS*	+<0.001
α-1-Antitrypsin (D):				
Low vs. Normal	ns	NS	--	ns
High vs. Normal	NS	--	ns	NS
α-2-Macroglobulin (C)	ns	ns	ns	ns
α-2-Macroglobulin (D)	ns	ns	ns	NS
Apolipoprotein B (C)	ns	–0.048	ns	NS
Apolipoprotein B (D)	ns*	ns	–0.005	NS
C3 Complement (C)[a]	NS	NS	ns	NS
C3 Complement (D)	ns	ns	ns	NS
C4 Complement (C)[a]	ns	–0.017	NS	ns
C4 Complement (D)	NS	NS	--	--
Haptoglobin (C)	+0.003	NS	NS	+0.016
Haptoglobin (D)	+0.020	NS	NS	NS*
Transferrin (C)[a]	+0.037	NS	NS	NS*
Transferrin (D)	–0.027	ns*	ns	ns

Table 13-76. Summary of Group Analysis (Model 1) for Gastrointestinal Variables (Ranch Hands vs. Comparisons) (Continued)

Note: NS or ns: Not significant (p>0.10).
NS* or ns*: Marginally significant (0.05<p≤0.10).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00 for discrete analysis; difference of means nonnegative for continuous analysis.
–: Relative risk <1.00 for discrete analysis; difference of means negative for continuous analysis.
--: Analysis not performed because of the sparse number of participants with an abnormality.
[a] Negative difference considered adverse for this variable.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

13.4.2 Model 2: Initial Dioxin Analysis

Model 2 analyses of medical records variables revealed a significant positive association between initial dioxin and other liver disorders.

Adjusted Model 2 analysis of the laboratory examination variables revealed a significant positive association between initial dioxin and the discrete form of ALT. A significant inverse association was seen between initial dioxin and the discrete form of HDL cholesterol in the adjusted analysis.

The results of all unadjusted and adjusted Model 2 analyses are summarized in Table 13-77.

Table 13-77. Summary of Initial Dioxin Analysis (Model 2) for Gastrointestinal Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Uncharacterized Hepatitis (D)	NS	NS
Jaundice (Unspecified) (D)	NS	NS
Chronic Liver Disease and Cirrhosis (Alcohol-related) (D)	NS	NS
Chronic Liver Disease and Cirrhosis (Non-alcohol-related) (D)	NS	NS
Liver Abscess and Sequelae of Chronic Liver Disease (D)	NS	NS
Enlarged Liver (Hepatomegaly) (D)	ns	ns
Other Liver Disorders (D)	NS	+0.022
Physical Examination		
Current Hepatomegaly (D)	ns	ns
Laboratory		
AST (C)	NS	NS
AST (D)	NS	NS
ALT (C)	NS	NS
ALT (D)	NS	+0.049
GGT (C)	NS	NS
GGT (D)	NS	NS
Alkaline Phosphatase (C)	ns	ns*
Alkaline Phosphatase (D)	ns	NS
Total Bilirubin (C)	ns	NS

Table 13-77. Summary of Initial Dioxin Analysis (Model 2) for Gastrointestinal Variables (Ranch Hands Only) (Continued)

Variable	Unadjusted	Adjusted
Total Bilirubin (D)	ns	ns
Direct Bilirubin (D)	--	--
Lactic Dehydrogenase (C)	ns	NS
Lactic Dehydrogenase (D)	ns	ns
Cholesterol (C)	+0.005	NS
Cholesterol (D)	+0.036	NS*
HDL Cholesterol (C)[a]	ns	NS
HDL Cholesterol (D)	ns	−0.029
Cholesterol-HDL Ratio (C)	+0.003	NS
Cholesterol-HDL Ratio (D)	+0.002	NS
Triglycerides (C)	NS	NS
Triglycerides (D)	NS	ns
Creatine Phosphokinase (C)	NS	ns
Creatine Phosphokinase (D)	NS	NS
Serum Amylase (C)	ns*	ns*
Serum Amylase (D)	ns	NS
Antibodies for Hepatitis A (D)	ns	NS
Serological Evidence of Prior Hepatitis B Infection (D)	NS	ns
Current Hepatitis B (D)	ns	ns
Antibodies for Hepatitis C (D)	ns	ns
Antibodies for Hepatitis D (D)	--	--
Stool Hemoccult (D)	ns	ns
Prealbumin (C)[a]	ns	ns
Prealbumin (D)	NS	NS*
Albumin (C)[a]	NS	ns
Albumin (D)	--	--
α-1-Acid Glycoprotein (C)	NS	ns*
α-1-Acid Glycoprotein (D)	NS	ns
α-1-Antitrypsin (C)	NS*	NS
α-1-Antitrypsin (D):		
Low vs. Normal	ns	ns
High vs. Normal	NS	ns
α-2-Macroglobulin (C)	ns	NS
α-2-Macroglobulin (D)	NS	NS*
Apolipoprotein B (C)	+0.009	NS
Apolipoprotein B (D)	NS*	NS
C3 Complement (C)[a]	+0.023	NS
C3 Complement (D)	NS	NS
C4 Complement (C)[a]	ns	ns
C4 Complement (D)	--	--
Haptoglobin (C)	NS	ns
Haptoglobin (D)	NS	ns
Transferrin (C)[a]	NS	ns
Transferrin (D)	ns	ns

Table 13-77. Summary of Initial Dioxin Analysis (Model 2) for Gastrointestinal Variables (Ranch Hands Only) (Continued)

Note: NS or ns: Not significant ($p>0.10$).
NS* or ns*: Marginally significant ($0.05<p\leq 0.10$).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00 for discrete analysis; slope nonnegative for continuous analysis.
–: Relative risk <1.00 for discrete analysis.
--: Analysis not performed because of the sparse number of Ranch Hands with an abnormality.
[a] Negative slope considered adverse for this variable.

P-value given if $p\leq 0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or slope nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

13.4.3 Model 3: Categorized Dioxin Analysis

Adjusted Model 3 analyses revealed a significantly higher percentage of other liver disorders among Ranch Hands in the high dioxin category than among Comparisons.

The adjusted results of the Ranch Hands in the high dioxin category versus Comparisons contrast revealed Ranch Hands had significantly higher mean levels of GGT, triglycerides, α-1-antitrypsin, and transferrin than Comparisons. The discrete analyses for AST, triglycerides, and prealbumin were also significant, with Ranch Hands in the high dioxin category having a higher prevalence of abnormal values than Comparisons. In addition, significantly less serological evidence of prior hepatitis B and low transferrin levels were noted in Ranch Hands in the high dioxin category than in Comparisons.

The adjusted result of the contrast between Ranch Hands in the low and high dioxin categories combined versus Comparisons revealed that Ranch Hands had significantly higher mean levels of ALT, GGT, α-1-antitrypsin, haptoglobin, and transferrin than Comparisons. The discrete analyses for AST and triglycerides were also significant, with Ranch Hands in the low and high dioxin categories combined having a greater prevalence of high values than Comparisons. In addition, significantly less serological evidence of prior hepatitis B and low transferrin levels were noted in the Ranch Hands in the low and high dioxin categories combined than in Comparisons.

The adjusted analyses also found several significant differences for the contrast between Ranch Hands in the background dioxin category versus Comparisons. Ranch Hands had significantly higher mean levels of alkaline phosphatase, α-1-antitrypsin, and haptoglobin than Comparisons. The discrete analyses for HDL cholesterol and haptoglobin were also significant, with Ranch Hands in the background dioxin category having a higher prevalence of abnormal values than Comparisons. In addition, significantly fewer Ranch Hands in the background dioxin category had serological evidence of prior hepatitis B and high apolipoprotein B levels than did Comparisons.

The results of all unadjusted and adjusted Model 3 analyses are summarized in Table 13-78.

Table 13-78. **Summary of Categorized Dioxin Analysis (Model 3) for Gastrointestinal Variables (Ranch Hands vs. Comparisons)**

Variable	UNADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Medical Records				
Uncharacterized Hepatitis (D)	NS	ns	NS	NS
Jaundice (Unspecified) (D)	NS	−0.017	ns*	−0.001
Chronic Liver Disease and Cirrhosis (Alcohol-related) (D)	ns	NS	NS	NS
Chronic Liver Disease and Cirrhosis (Non-alcohol-related) (D)	NS	NS	NS	NS
Liver Abscess and Sequelae of Chronic Liver Disease (D)	ns	ns	NS	NS
Enlarged Liver (Hepatomegaly) (D)	ns	ns	NS	ns
Other Liver Disorders (D)	NS	NS	+0.009	+0.042
Physical Examination				
Current Hepatomegaly (D)	NS	NS	NS	NS
Laboratory				
AST (C)	ns	NS	NS	NS
AST (D)	ns	NS	NS*	NS*
ALT (C)	ns	NS	+0.027	+0.041
ALT (D)	ns	NS	+0.015	NS*
GGT (C)	ns	NS	+0.003	+0.007
GGT (D)	ns	NS	NS	NS*
Alkaline Phosphatase (C)	NS	NS*	NS	NS*
Alkaline Phosphatase (D)	NS	ns	NS	NS
Total Bilirubin (C)	NS	ns	ns	ns
Total Bilirubin (D)	ns	NS	ns	ns
Direct Bilirubin (D)	ns	--	--	--
Lactic Dehydrogenase (C)	NS	ns	NS	NS
Lactic Dehydrogenase (D)	NS	ns	ns	ns
Cholesterol (C)	ns	ns	+0.032	NS
Cholesterol (D)	ns	ns	+0.023	NS
HDL Cholesterol (C)[a]	NS	NS	ns	ns
HDL Cholesterol (D)	NS	NS	ns	NS
Cholesterol-HDL Ratio (C)	ns*	ns	+0.005	NS
Cholesterol-HDL Ratio (D)	ns	ns	+0.002	NS
Triglycerides (C)	ns	ns	+<0.001	+0.023
Triglycerides (D)	ns*	NS	+<0.001	+0.006
Creatine Phosphokinase (C)	NS	NS	NS	NS
Creatine Phosphokinase (D)	ns	ns	NS	ns
Serum Amylase (C)	ns	+0.019	ns	NS
Serum Amylase (D)	ns	NS	ns	NS
Antibodies for Hepatitis A (D)	ns	NS	NS	NS
Serological Evidence of Prior Hepatitis B Infection (D)	−<0.001	ns	ns	ns
Current Hepatitis B (D)	--	NS	--	NS
Antibodies for Hepatitis C (D)	ns	ns	ns	ns
Antibodies for Hepatitis D (D)	--	--	--	--
Stool Hemoccult (D)	ns	NS	ns	ns

Table 13-78. Summary of Categorized Dioxin Analysis (Model 3) for Gastrointestinal Variables (Ranch Hands vs. Comparisons) (Continued)

Variable	UNADJUSTED: Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Prealbumin (C)[a]	ns	ns	NS	ns
Prealbumin (D)	NS	ns	NS*	NS
Albumin (C)[a]	NS	ns*	NS	ns
Albumin (D)	ns	ns	ns	ns*
α-1-Acid Glycoprotein (C)	ns	NS	+0.045	NS
α-1-Acid Glycoprotein (D)	NS	NS	NS	NS
α-1-Antitrypsin (C)	NS	NS	+<0.001	+0.001
α-1-Antitrypsin (D):				
Low vs. Normal	NS	ns	ns	ns
High vs. Normal	NS	NS	NS	NS
α-2-Macroglobulin (C)	ns	ns	ns	ns
α-2-Macroglobulin (D)	ns*	ns	NS	ns
Apolipoprotein B (C)	ns*	ns	NS*	NS
Apolipoprotein B (D)	−0.017	ns	NS	ns
C3 Complement (C)[a]	ns	NS	+0.003	+0.013
C3 Complement (D)	NS	ns	ns	ns*
C4 Complement (C)[a]	ns	NS	NS	NS
C4 Complement (D)	NS	ns	ns	ns
Haptoglobin (C)	NS	NS*	+0.001	+0.001
Haptoglobin (D)	NS	NS	+0.023	+0.015
Transferrin (C)[a]	NS	NS	+0.010	+0.019
Transferrin (D)	ns	ns	−0.039	ns*

Note: NS or ns: Not significant (p>0.10).
NS* or ns*: Marginally significant (0.05<p≤0.10).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00 for discrete analysis; difference of means nonnegative for continuous analysis.
−: Relative risk <1.00 for discrete analysis.
--: Analysis not performed because of the sparse number of participants with an abnormality.
[a] Negative difference considered adverse for this variable.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Variable	ADJUSTED: Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Medical Records				
Uncharacterized Hepatitis (D)	NS	NS	NS	NS
Jaundice (Unspecified) (D)	ns	--	ns*	--
Chronic Liver Disease and Cirrhosis (Alcohol-related) (D)	NS	ns	ns	ns

Table 13-78. Summary of Categorized Dioxin Analysis (Model 3) for Gastrointestinal Variables (Ranch Hands vs. Comparisons) (Continued)

Variable	ADJUSTED Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Chronic Liver Disease and Cirrhosis (Non-alcohol-related) (D)	NS	NS	NS	NS
Liver Abscess and Sequelae of Chronic Liver Disease (D)	--	--	NS	--
Enlarged Liver (Hepatomegaly) (D)	ns	ns	NS	ns
Other Liver Disorders (D)	NS	NS	+0.009	NS*
Physical Examination				
Current Hepatomegaly (D)	NS	NS	NS	NS
Laboratory				
AST (C)	ns	NS	NS	NS*
AST (D)	ns	NS	+0.024	+0.041
ALT (C)	ns	NS*	NS*	+0.026
ALT (D)	ns	NS	NS*	NS*
GGT (C)	ns	NS	+0.006	+0.006
GGT (D)	ns	NS	NS	NS*
Alkaline Phosphatase (C)	+0.008	NS*	ns	NS
Alkaline Phosphatase (D)	NS	ns	NS	NS
Total Bilirubin (C)	ns	ns	NS	NS
Total Bilirubin (D)	ns	NS	ns	ns
Direct Bilirubin (D)	NS	--	--	--
Lactic Dehydrogenase (C)	NS	ns	NS	NS
Lactic Dehydrogenase (D)	NS	ns	ns	ns
Cholesterol (C)	ns	ns	NS	NS
Cholesterol (D)	ns	NS	NS*	NS
HDL Cholesterol (C)[a]	NS	NS	NS	NS
HDL Cholesterol (D)	+0.049	NS	ns	ns
Cholesterol-HDL Ratio (C)	ns	ns	NS	NS
Cholesterol-HDL Ratio (D)	NS	ns	NS	NS
Triglycerides (C)	ns	NS	+0.013	NS*
Triglycerides (D)	ns	NS	+0.009	+0.012
Creatine Phosphokinase (C)	ns	NS	NS	NS
Creatine Phosphokinase (D)	ns	ns	NS	ns
Serum Amylase (C)	ns	NS*	ns	NS
Serum Amylase (D)	ns	NS	NS	NS
Antibodies for Hepatitis A (D)	ns	ns	ns	ns
Serological Evidence of Prior Hepatitis B Infection (D)	–0.004	ns	–0.021	–0.012
Current Hepatitis B (D)	--	NS	--	--
Antibodies for Hepatitis C (D)	ns	ns	ns	ns
Antibodies for Hepatitis D (D)	--	--	--	--
Stool Hemoccult (D)	ns	NS	ns	ns
Prealbumin (C)[a]	ns	NS	NS	NS
Prealbumin (D)	NS	ns	+0.021	NS
Albumin (C)[a]	NS	ns	NS	ns
Albumin (D)	ns	--	--	--
α-1-Acid Glycoprotein (C)	ns	NS	NS	NS
α-1-Acid Glycoprotein (D)	NS	NS	NS	NS
α-1-Antitrypsin (C)	+0.024	NS	+0.011	+0.020

Table 13-78. Summary of Categorized Dioxin Analysis (Model 3) for Gastrointestinal Variables (Ranch Hands vs. Comparisons) (Continued)

	ADJUSTED			
Variable	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
α-1-Antitrypsin (D):				
Low vs. Normal	ns	ns	NS	NS
High vs. Normal	NS	NS	NS	NS
α-2-Macroglobulin (C)	ns	ns	NS	ns
α-2-Macroglobulin (D)	ns*	ns	NS	ns
Apolipoprotein B (C)	ns	ns	NS	ns
Apolipoprotein B (D)	−0.050	ns	ns	ns
C3 Complement (C)[a]	ns	NS	NS	NS
C3 Complement (D)	NS	ns	ns	ns*
C4 Complement (C)[a]	ns	NS	ns	ns
C4 Complement (D)	NS	--	--	--
Haptoglobin (C)	+0.014	NS	NS	+0.036
Haptoglobin (D)	+0.042	NS	NS	NS
Transferrin (C)[a]	NS	NS	+0.050	+0.032
Transferrin (D)	ns	ns	−0.045	−0.039

Note: NS or ns: Not significant (p>0.10).
NS* or ns*: Marginally significant (0.05<p≤0.10).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00 for discrete analysis; difference of means nonnegative for continuous analysis.
−: Relative risk <1.00 for discrete analysis.
--: Analysis not performed because of the sparse number of participants with an abnormality.
[a] Negative difference considered adverse for this variable.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

13.4.4 Model 4: 1987 Dioxin Level Analysis

The Model 4 analysis revealed a significant inverse association between jaundice and 1987 dioxin.

Many significant associations between the laboratory examination variables and 1987 dioxin levels were seen in the Model 4 analyses. In both the continuous and discrete forms, the hepatic enzymes ALT, AST, and GGT revealed significant, positive associations with 1987 dioxin. Alkaline phosphatase revealed significant inverse associations with 1987 dioxin in both the continuous and discrete analyses.

For the lipid and carbohydrate indices, the Model 4 continuous and discrete analyses detected significant positive associations with the cholesterol-HDL ratio and triglycerides. A significant inverse relation was seen between 1987 dioxin and HDL cholesterol for both discrete and continuous analyses.

Analysis of creatine phosphokinase in both its continuous and discrete forms revealed a significant positive association with 1987 dioxin. In addition, a significant inverse association between 1987 dioxin and the continuous form of serum amylase was found.

The adjusted results of the protein profile variables yielded several significant findings. A significant inverse association between 1987 dioxin and the continuous form of α-1-acid glycoprotein and a significant positive association between 1987 dioxin and C3 complement in its continuous form were found. The discrete analysis showed more Ranch Hands than Comparisons with a high α-2-macroglobulin level, and more Comparisons than Ranch Hands with low C3 complement and C4 complement levels.

The results of all Model 4 analyses are summarized in Table 13-79.

Table 13-79. Summary of 1987 Dioxin Analysis (Model 4) for Gastrointestinal Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Uncharacterized Hepatitis (D)	ns	ns
Jaundice (Unspecified) (D)	–<0.001	–<0.001
Chronic Liver Disease and Cirrhosis (Alcohol-related) (D)	NS	NS
Chronic Liver Disease and Cirrhosis (Non-alcohol-related) (D)	NS	NS
Liver Abscess and Sequelae of Chronic Liver Disease (D)	NS	NS
Enlarged Liver (Hepatomegaly) (D)	ns	ns
Other Liver Disorders (D)	NS*	NS*
Physical Examination		
Current Hepatomegaly (D)	NS	NS
Laboratory		
AST (C)	+0.033	+0.002
AST (D)	+0.008	+0.002
ALT (C)	+<0.001	+<0.001
ALT (D)	+0.001	+<0.001
GGT (C)	+0.002	+0.003
GGT (D)	+0.034	+0.012
Alkaline Phosphatase (C)	ns	–0.003
Alkaline Phosphatase (D)	ns	–0.020
Total Bilirubin (C)	ns	NS
Total Bilirubin (D)	ns	ns
Direct Bilirubin (D)	ns	ns
Lactic Dehydrogenase (C)	NS	NS
Lactic Dehydrogenase (D)	NS	NS
Cholesterol (C)	+0.009	NS
Cholesterol (D)	+0.025	NS
HDL Cholesterol (C)[a]	–<0.001	–0.037
HDL Cholesterol (D)	ns	–0.029
Cholesterol-HDL Ratio (C)	+<0.001	+0.006
Cholesterol-HDL Ratio (D)	+<0.001	+0.025
Triglycerides (C)	+<0.001	+<0.001
Triglycerides (D)	+<0.001	+0.001
Creatine Phosphokinase (C)	NS*	+0.011
Creatine Phosphokinase (D)	NS	+0.043
Serum Amylase (C)	–0.035	–0.003
Serum Amylase (D)	ns	ns
Antibodies for Hepatitis A (D)	NS	NS
Serological Evidence of Prior Hepatitis B Infection (D)	+0.023	NS
Current Hepatitis B (D)	NS	NS

Table 13-79. Summary of 1987 Dioxin Analysis (Model 4) for Gastrointestinal Variables (Ranch Hands Only) (Continued)

Variable	Unadjusted	Adjusted
Antibodies for Hepatitis C (D)	ns	ns
Antibodies for Hepatitis D (D)	--	--
Stool Hemoccult (D)	NS	NS
Prealbumin (C)[a]	ns	ns
Prealbumin (D)	NS	NS
Albumin (C)[a]	ns	ns
Albumin (D)	ns	ns
α-1-Acid Glycoprotein (C)	NS	−0.049
α-1-Acid Glycoprotein (D)	NS	ns
α-1-Antitrypsin (C)	NS	ns*
α-1-Antitrypsin (D):		
Low vs. Normal	ns	ns
High vs. Normal	ns	ns
α-2-Macroglobulin (C)	ns	ns
α-2-Macroglobulin (D)	+0.020	+0.014
Apolipoprotein B (C)	+0.002	NS
Apolipoprotein B (D)	+0.017	NS
C3 Complement (C)[a]	+<0.001	+<0.001
C3 Complement (D)	−0.011	−0.004
C4 Complement (C)[a]	NS*	NS
C4 Complement (D)	−0.033	−0.024
Haptoglobin (C)	NS	ns
Haptoglobin (D)	NS	ns
Transferrin (C)[a]	NS*	NS
Transferrin (D)	NS	NS

Note: NS or ns: Not significant ($p>0.10$).
NS* or ns*: Marginally significant ($0.05<p\leq0.10$).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00 for discrete analysis; slope nonnegative for continuous analysis.
−: Relative risk <1.00 for discrete analysis; slope negative for continuous analysis.
--: Analysis not performed because of the sparse number of Ranch Hands with an abnormality.
[a] Negative slope considered adverse for this variable.

P-value given if $p\leq0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or slope nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

13.5 CONCLUSION

The gastrointestinal assessment was based on eight disorders as determined from a review and verification of each participant's medical records, a physical examination determination of hepatomegaly, and 29 laboratory measurements or indices. The laboratory parameters included measurements of hepatic enzyme activity, hepatobiliary function, lipid and carbohydrate indices, and a protein profile. In addition, the presence of hepatitis and fecal occult blood was investigated.

Analyses of Ranch Hands versus Comparisons showed higher mean levels of alkaline phosphatase, α-1-antitrypsin, and haptoglobin in Ranch Hands than in Comparisons. In addition, significantly more Ranch Hands than Comparisons had high haptoglobin levels. A review of medical records showed a positive association between initial dioxin and other liver disorders. Twelve percent of the participants with the other liver disorders condition had nonspecific laboratory test elevations. A significant association between initial dioxin and high levels of AST also was revealed.

Analyses of categorized dioxin revealed a significantly higher percentage of other liver disorders among Ranch Hands in the high dioxin category than among Comparisons. Higher mean levels of GGT, triglycerides, and α-1-antitrypsin were observed in Ranch Hands in the high dioxin category than in Comparisons. Ranch Hands in the high dioxin category had a greater prevalence of abnormal AST, triglyceride, and prealbumin levels than did Comparisons.

Many significant associations between the laboratory examination variables and 1987 dioxin levels were observed. In both the continuous and discrete forms, the hepatic enzymes ALT, AST, and GGT revealed significant, positive associations with 1987 dioxin. In addition, significant positive associations between 1987 dioxin and the cholesterol-HDL ratio, triglycerides, and creatine phosphokinase were present.

In summary, the analysis of the 1997 follow-up data reflected patterns that have been observed and documented in prior examinations. A composite category of disease named "other liver disorders" exhibited a dose-response relation with dioxin. Isolated group differences exist, but 1987 dioxin levels are strongly related to hepatic enzymes such as AST, ALT, and GGT, and to lipid-related health indices such as cholesterol, HDL, and triglycerides. These results are consistent with a dose-response effect and may be related to unknown subclinical effects of dioxin. Although hepatic enzymes showed an association with dioxin, there was no evidence of an increase in overt liver disease. The relation between other liver disorders and herbicide exposure and dioxin levels will be described in greater detail in a separate report.

REFERENCES

1. Poiger, H., and C. Schlatter. 1986. Pharmacokinetics of 2,3,7,8-TCDD in man. *Chemosphere* 15:1489-94.

2. Kancir, C. B., C. Andersen, and A. S. Olesen. 1988. Marked hypocalcemia in a fatal poisoning with chlorinated phenoxy acid derivatives. *Clinical Toxicology* 26:257-64.

3. Meulenbelt, J., J. H. Zwaveling, P. van Zoonen, and N. C. Notermans. 1988. Acute MCPP intoxication: Report of two cases. *Human Toxicology* 7:289-92.

4. McNulty, W. P. 1977. Toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin for Rhesus monkeys: Brief report. *Bulletin of Environmental Contamination and Toxicology* 18:108-9.

5. Olson, J. R., M. A. Holscher, and R. A. Neal. 1980. Toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin in the golden Syrian hamster. *Toxicology and Applied Pharmacology* 55:67-78.

6. Palmer, J. S., and R. D. Radeleff. 1964. The toxicologic effects of certain fungicides and herbicides on sheep and cattle. *Annals of the New York Academy of Sciences* 11:729-36.

7. Goldstein, J. A., P. Hickman, H. Bergman, and J. G. Vos. 1973. Hepatic porphyria induced by 2,3,7,8-tetrachlorodibenzo-p-dioxin in the mouse. *Research Communications in Chemical Pathology and Pharmacology* 6:919.

8. Madhukar, B. V., and F. Matsumura. 1981. Difference in the nature of induction of mixed-function oxidase systems of the rat liver among phenobarbital, DDT, 3-methylcholanthrene, and TCDD. *Toxicology and Applied Pharmacology* 61:110-8.

9. Brooks, A. L., S. W. Jordan, K. K. Bose, J. Smith, and D. C. Allison. 1988. The cytogenetic and hepatotoxic effects of dioxin on mouse liver cells. *Cell Biology and Toxicology* 4:31-40.

10. Potter, C. L., I. G. Sipes, and D. H. Russell. 1983. Hypothyroxinemia and hypothermia in rats in response to 2,3,7,8-tetrachlorodibenzo-p-dioxin administration. *Toxicology and Applied Pharmacology* 69:89-95.

11. Theobald, H. M., G. B. Ingall, T. A. Mably, and R. E. Peterson. 1991. Response of the antral mucosa of the rat stomach to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Toxicology and Applied Pharmacology* 108:167-79.

12. Norback, D. H., and J. R. Allen. 1973. Biological responses of the nonhuman primate, chicken, and rat to chlorinated dibenzo-p-dioxin ingestion. *Environmental Health Perspectives* 5:233-40.

13. Becker, G. M., and W. P. McNulty. 1984. Gastric epithelial cell proliferation in monkeys fed 3,4,3,4-tetrachlorobiphenyl. *Journal of Pathology* 143:267-74.

14. Richter, E., G. Hunder, and W. Forth. 1992. Inhibition of intestinal glucose absorption in rats treated with 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Veterinary and Human Toxicology* 34:123-6.

15. Shen, E. S., S. I. Gutman, and J. R. Olson. 1991. Comparison of 2,3,7,8-tetrachlorodibenzo-p-dioxin-mediated hepatotoxicity in C57BL/6J and DBA/2J mice. *Journal of Toxicology and Environmental Health* 32(4):367-81.

16. Piper, W. N., R. Q. Rose, and P. J. Gehring. 1973. Excretion and tissue distribution of 2,3,7,8-tetrachlorodibenzo-p-dioxin in the rat. *Environmental Health Perspectives* 5:241-4.

17. Allen, J. R., J. P. Van Miller, and D. H. Norback. 1977. Tissue distribution, excretion, and biological effects of (14C) tetrachlorodibenzo-p-dioxin in rats. *Food and Cosmetic Toxicology* 15:401-10.

18. Tsuda, S., A. Rosenberg, and T. Nakatsugawa. 1988. Translobular uptake patterns of environmental toxicants in the rat liver. *Bulletin of Environmental Contamination and Toxicology* 40:410-7.

19. Lakshman, M. R., B. S. Campbell, S. J. Chirtel, N. Ekarohita, and M. Ezekiel. 1986. Studies on the mechanism of absorption and distribution of 2,3,7,8-tetrachlorodibenzo-p-dioxin in the rat. *Journal of Pharmacology and Experimental Therapeutics* 239:673-7.

20. Pohjanvirta, R., T. Vartiainen, A. Uusi-Rauva, J. Monkkonen, and J. Tuomisto. 1990. Tissue distribution, metabolism, and excretion of 14C-TCDD in a TCDD-susceptible and a TCDD-resistant rat strain. *Pharmacology and Toxicology* 66:93-100.

21. Hagenmaier, H., T. Wiesmuller, G. Golor, R. Krowke, H. Helge, and D. Neubert. 1990. Transfer of various polychlorinated dibenzo-p-dioxins and dibenzofurans (PCDDs and PCDFs) via placenta and through milk in a marmoset monkey. *Archives of Toxicology* 64:601-15.

22. Gehring, P. J., and J. E. Betso. 1978. Phenoxy acids: effects and fate in mammals. *Ecology Bulletin* 27:122-33.

23. U. S. Environmental Protection Agency. 1984. Health assessment document for polychlorinated dibenzo-p-dioxins. Cincinnati, Ohio: EPA.

24. Dragan, Y. P., X. H. Xu, T. L. Goldsworthy, H. A. Campbell, R. R. Maronpot, and H. C. Pitot. 1992. Characterization of the promotion of altered hepatic foci by 2,3,7,8-tetrachlorodibenzo-p-dioxin in the female rat. *Carcinogenesis* 13(8):1389-95.

25. Kociba, R. J., D. G. Keyes, J. E. Beyer, R. M. Carreon, C. E. Wade, D. A. Dittenber, R. P. Kalnins, L. E. Frauson, C. N. Park, S. D. Barnard, R. A. Hummel, and C. G. Humiston. 1978. Results of a two-year chronic toxicity and oncogenicity study of 2,3,7,8-tetrachlorodibenzo-p-dioxin in rats. *Toxicology and Applied Pharmacology* 46:279-303.

26. Goodman, D. G., and R. M. Sauer. 1992. Hepatotoxicity and carcinogenicity in female Sprague-Dawley rats treated with 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD): a pathology working group reevaluation. *Regulatory Toxicology and Pharmacology* 15(3):245-52.

27. National Toxicology Program. 1982. Bioassay of 2,3,7,8-tetrachlorodibenzo-p-dioxin for possible carcinogenicity (Gavage study). Technical Report Series No. 209. National Toxicology Program, Research Triangle Park, North Carolina.

28. Mably, T. A., H. M. Theobald, G. B. Ingall, and R. E. Peterson. 1990. Hypergastrinemia is associated with decreased gastric acid secretion in 2,3,7,8-tetrachlorodibenzo-p-dioxin-treated rats. *Toxicology and Applied Pharmacology* 106:518-28.

29. Al-Turk, W. A., M. A. Shara, H. Mohammadpour, and S. J. Stohs. 1988. Dietary iron and 2,3,7,8-tetrachlorodibenzo-p-dioxin-induced alterations in hepatic lipid peroxidation glutathione content and body weight. *Drug and Chemical Toxicology* 11:55-70.

30. Shara, M. A., and S. J. Stohs. 1987. Biochemical and toxicological effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Archives of Environmental Contamination and Toxicology* 16:599-606.

31. Al-Bayati, Z. A. F., and S. J. Stohs. 1991. The possible role of phospholipase A2 in hepatic microsomal lipid peroxidation induced by 2,3,7,8-tetrachlorodibenzo-p-dioxin in rats. *Archives of Environmental Contamination and Toxicology* 20(3):361-5.

32. Al-Bayati, Z. A. F., and S. J. Stohs. 1987. The role of iron in 2,3,7,8-tetrachlorodibenzo-p-dioxin-induced lipid peroxidation by rat liver microsomes. *Toxicology Letters* 38:115-21.

33. Lakshman, M. R., P. Ghosh, and S. J. Chirtel. 1991. Mechanism of action of 2,3,7,8-tetrachlorodibenzo-p-dioxin on intermediary metabolism in the rat. *Journal of Pharmacology and Experimental Therapeutics* 258(1):317-9.

34. Kohli, K. K., and J. A. Goldstein. 1981. Effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin on hepatic and renal prostaglandin synthetase. *Life Sciences* 19:299-305.

35. Lakshman, M. R., S. J. Chirtel, L. L. Chambers, and P. J. Coutlakis. 1989. Effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin on lipid synthesis and lipogenic enzymes in the rat. *Journal of Pharmacology and Experimental Therapeutics* 248:62-6.

36. Martin, J. V. 1984. Lipid abnormalities in workers exposed to dioxin. *British Journal of Industrial Medicine* 41:254-6.

37. Lakshman, M. R., B. S. Campbell, S. J. Chirtel, and N. Ekarohita. 1988. Effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on de-novo fatty acid and cholesterol synthesis in the rat. *Lipids* 23:904-6.

38. Cantoni, L., A. Graziani, M. Rizzardini, and M. C. Saletti. 1986. Porphyrinogenic effect of hexachlorobenzene and 2,3,7,8-tetrachlorodibenzo-para-dioxin: Is an inhibitor involved in uroporphyrinogen decarboxylase inactivation? *IARC Scientific Publications* No. 77:449-56.

39. Goldstein, J. A., P. Hickman, and D. L. Jue. 1974. Experimental hepatic porphyria induced by polychlorinated biphenyls. *Toxicology and Applied Pharmacology* 27:437.

40. Bleiberg, J., M. Wallen, R. Brodkin, and I. L. Applebaum. 1964. Industrially acquired porphyria. *Archives of Dermatology* 89:793-7.

41. Jirasek, L., J. Kalensky, K. Kubec, J. Pazderova, and E. Lukas. 1974. In Part 2, Acne chlorina, porphyria cutanea tarda and other manifestations of general intoxication during the manufacture of herbicides. *Czech Dermatology* 49:145-57.

42. Lucier, G. W., R. C. Rumbaugh, Z. McCoy, R. Hass, D. Harvan, and P. Albro. 1986. Ingestion of soil contaminated with 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) alters hepatic enzyme activities in rats. *Fundamental and Applied Toxicology* 6:364-71.

43. Ideo, G., G. Bellati, A. Bellobuono, A. Mocarelli, P. Marocchi, A. and P. Brambilla. 1982. Increased urinary d-glucaric acid excretion by children living in an area polluted with tetrachlorodibenzodioxin (TCDD). *Clinica Chimica Acta* 120:273-83.

44. Ideo, G., G. Bellati, A. Bellobuono, and L. Bisanti. 1985. Urinary d-glucaric acid excretion in the Seveso area, polluted by tetrachlorodibenzo-p-dioxin (TCDD): Five years of experience. *Environmental Health Perspectives* 60:151-7.

45. U.S. Centers for Disease Control. Health status of Vietnam veterans. In Part 2, Physical health. The Centers for Disease Control Vietnam experience study. *Journal of the American Medical Association* 259:2708-14.

46. Hoffman, R. E., P. A. Stehr-Green, K. B. Webb, G. Evans, A. P. Knutsen, W. F. Schramm, J. L. Staake, B. B. Gibson, and K. K. Steinberg. 1986. Health effects of long-term exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Journal of the American Medical Association* 255:2031-8.

47. Calvert, G. M., R. W. Hornung, M. H. Sweeney, M. A. Fingerhut, and W. E. Halperin. 1992. Hepatic and gastrointestinal effects in an occupational cohort exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Journal of the American Medical Association* 267(16):2209-14.

48. Caramaschi, F., G. Del Corno, C. Favaretti, S. E. Giambelluca, E. Montesarchio, and G. M. Fara. 1981. Chloracne following environmental contamination by TCDD in Seveso, Italy. *International Journal of Epidemiology* 10:135-43.

49. Suskind, R. R., and V. S. Hertzberg. 1984. Human health effects of 2,4,5-T and its toxic contaminants. *Journal of the American Medical Association* 251:2372-80.

50. Bond, G. G., M. G. Ott, F. E. Brenner, and R. R. Cook. 1983. Medical and morbidity surveillance findings among employees potentially exposed to TCDD. *British Journal of Industrial Medicine* 40:318-24.

51. Oliver, R. M. 1975. Toxic effects of 2,3,7,8-tetrachlorodibenzo 1,4-dioxin in laboratory workers. *British Journal of Industrial Medicine* 32:49-53.

52. Reggiani, G. 1980. Acute human exposure to TCDD in Seveso, Italy. *Journal of Toxicology and Environmental Health* 6:27-43.

53. May, G. 1973. Chloracne from the accidental production of tetrachlorodibenzodioxin. *British Journal of Industrial Medicine* 30:276-83.

54. Mocarelli, P., A. Marocchi, P. Brambilla, P. Gerthoux, D. S. Young, and N. Mantel. 1986. Clinical laboratory manifestations of exposure to dioxin in children. *Journal of the American Medical Association* 256:2687-95.

55. May, G. 1982. Tetrachlorodibenzodioxin: A survey of subjects ten years after exposure. *British Journal of Industrial Medicine* 39:128-35.

56. Moses, M., R. Lilis, K. D. Crow, J. Thornton, A. Fischbein, H. A. Anderson, and I. J. Selikoff. 1984. Health status of workers with past exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin in the manufacture of 2,4,5-trichlorophenoxyacetic acid: Comparison of findings with and without chloracne. *American Journal of Industrial Medicine* 5:161-82.

57. Assennato, G., P. Cannatalli, and I. Ghezzi. 1986. Health surveillance of a potential TCDD-exposed industrial population in Seveso: Pattern of some liver-related biochemical indicators. In Occupational and Environmental Chemical Hazards: Cellular and Biochemical Indices for Monitoring Toxicity. Eds. V. Foa, E. A. Emmett, M. Maroni, and A. Colombi. Chichester, England: Ellis Horwood Limited.

58. Webb, K. B., R. G. Evans, A. P. Knutsen, S. T. Roodman, D. W. Roberts, W. F. Schramm, B. B. Gibson, J. S. Andrews Jr., L. L. Needham, and D. G. Patterson. 1989. Medical evaluation of subjects with known body levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Journal of Toxicology and Environmental Health* 28:183-93.

59. Von Benner, A., L. Edler, K. Mayer, and A. Zober. 1994. 'Dioxin' investigation program of the chemical industry professional association. *Arbeitsmedizin Sozialmedizin Praventivmedizin* 29:11-6.

60. Ott, M. G., A. Zober, and C. Germann. 1994. Laboratory results for selected target organs in 138 individuals occupationally exposed to TCDD. *Chemosphere* 29:2423-37.

61. Zober, A., M. G. Ott, and P. Messerer. 1994. Morbidity follow-up study of BASF employees exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) after a 1953 chemical reactor incident. *Occupational and Environmental Medicine* 51:479-86.

62. Tamburro, C. H. 1992. Chronic liver injury in phenoxy herbicide-exposed Vietnam veterans. *Environmental Research* 59:175-88.

63. Thomas, T. L., and H. K. Kang. 1990. Mortality and morbidity among Army Chemical Corps Vietnam veterans: A preliminary report. *American Journal of Industrial Medicine* 18:665-73.

64. Roegner, R. H., W. D. Grubbs, M. B. Lustik, A. S. Brockman, S. C. Henderson, D. E. Williams, W. H. Wolfe, J. E. Michalek, and J. C. Miner. 1991. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Serum Dioxin Analysis of 1987 Examination Results. NTIS: AD A 237 516-24. USAF School of Medicine, Brooks Air Force Base, Texas.

65. Grubbs, W. D., W. H. Wolfe, J. E. Michalek, D. E. Williams, M. B. Lustik, A. S. Brockman, S. C. Henderson, F. R. Burnett, R. G. Land, D. J. Osborne, V. K. Rocconi, M. E. Schreiber, J. C. Miner, G. L. Henriksen, and J. A. Swaby. 1995. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final Report. 1992 Followup Examination Results. NTIS: AD A 304 306, 304 308-316. USAF School of Medicine, Brooks Air Force Base, Texas.

66. Michalek, J. E., J. L. Pirkle, S. P. Caudill, R. C. Tripathi, D. G. Patterson Jr., and L. L. Needham. 1996. Pharmacokinetics of TCDD in Veterans of Operation Ranch Hand: 10-year Followup. *Journal of Toxicology and Environmental Health* 47:209-20.

67. Mausner, J. S., and A. K. Bahn. 1974. *Epidemiology – An Introductory Text.* Philadelphia: W. B. Saunders Company.

Table of Contents

List of Tables

14 CARDIOVASCULAR ASSESSMENT

14.1 INTRODUCTION

14.1.1 Background

Animal research into the cardiotoxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (dioxin) has focused on acute biochemical and functional abnormalities associated with high-level exposure. In one study (1), rats were found to have reductions in pulse and blood pressure 6 days after administration of 40 μg/kg of dioxin by gavage and were less responsive to the chronotropic effect of isoproterenol, a beta-agonist. The authors of the study, noting a 66-percent reduction in serum thyroxine, postulated a down regulation of beta-receptors associated with the hypothyroid state rather than a direct cardiotoxic effect. Their findings were consistent with other studies that documented changes in myocardial beta-receptors with reduced serum indices of thyroid function and decreased beta-adrenergic responsiveness to isoproterenol in the ventricular papillary muscle of guinea pigs (2). Experiments into the effects of dioxin on myocardial contractility in rat (3) and guinea pig (4) atrial muscle have yielded mixed results; the primary cardiotoxic effects remain uncertain.

The biochemical effects of dioxin on cardiac muscle have been the subject of several reports. An increase in lipid peroxidation and a decrease in superoxide dismutase activity were noted in the hearts of female rats after dioxin administration (1). Dose-dependent decreases in adipose tissue lipoprotein lipase activity and hepatic low-density lipoprotein binding occurred in rabbits (5) and other laboratory animals (6) in association with elevated serum triglycerides. Electron microscopic studies have documented pre-atherosclerotic lesions in the aortic arch in association with these biochemical abnormalities (5) and dioxin exposure has been associated with intravascular thrombosis in rats (7). Two recent studies provide evidence that the developing vascular endothelium of fish embryos may be a target organ for dioxin toxicity (8, 9).

Numerous studies have focused on the effects of dioxin toxicity on lipid metabolism in experimental animals and may be relevant to herbicide exposure as a risk factor for the development of heart disease in man. Dioxin-induced hyperlipidemia has been documented in rats (10, 11), guinea pigs (12), and rabbits (5).

Numerous epidemiological studies have investigated cardiovascular mortality and morbidity in populations exposed to dioxin by occupation and consequent to industrial accidents (13–22). Other reports have examined similar endpoints in veterans who served in the Vietnam War (23–35). Some occupational (13, 20) and veterans' studies (23, 25, 26, 28–31) cited have shown no increase in cardiovascular mortality associated with exposure to dioxin, and several have documented a significant reduction in risk (23, 26, 27). However, in the 1994 Air Force Health Study (AFHS) mortality update (36), the Ranch Hand nonflying enlisted personnel were found to be at higher risk for death associated with circulatory disease than the Comparison nonflying enlisted personnel. Most occupational studies have found no increased risk for the development of cardiovascular disease related to dioxin exposure (13–16, 20). In two reports of the 1976 Seveso, Italy, industrial accident, dioxin exposure was associated with statistically significant increases in mortality because of coronary, cerebrovascular, and hypertensive vascular disease (18, 19).

The latest morbidity follow-up study of BASF Corporation employees highly exposed to dioxin during a chemical reactor incident in 1953 has been published (21). Almost half of the study group had

extrapolated serum dioxin levels of more than 1,000 parts per trillion (ppt). Across all exposure categories, there was no significant increase in the incidence of ischemic heart disease.

A more recently published retrospective cohort study examined cardiovascular mortality in 1,189 German chemical workers who had significant dioxin exposure in the 1950s (37). In this study, exposure was verified and subjects stratified into deciles based on serum and adipose tissue dioxin levels. There was a slight reduction in mortality risk at the two lowest levels of exposure, but a clear pattern of increasing risk for all-cause cardiovascular mortality and, particularly, for that associated with ischemic heart disease. The dose-response trend for both causes of mortality was significant ($p \leq 0.01$).

The well-established roles of diabetes mellitus and lipid disorders as risk factors in the development of cardiovascular disease have generated considerable interest in the potential intermediary role these metabolic indices might have on cardiovascular outcomes associated with dioxin exposure. Data and results from this (35, 38) and other epidemiological studies (22, 37, 39–44) are considered in the Gastrointestinal Assessment chapter (Chapter 13) and the Endocrine Assessment chapter (Chapter 16).

Previous AFHS examinations have shown mixed results with respect to cardiovascular endpoints. In the baseline and 1987 follow-up examinations, manual examination of the pulses revealed an increased prevalence of pulse deficits in the Ranch Hand cohort relative to Comparisons (45, 46), results noted as well in studies of residents exposed to dioxin in Times Beach, Missouri (47, 48). In the 1985 AFHS follow-up examination, which incorporated Doppler peripheral vascular studies into the protocol, no significant group differences were found (49). When the 1987 examination data were analyzed relative to serum dioxin levels, Ranch Hand participants in one high exposure category had higher percentages of peripheral pulse abnormalities by manual examination than did Comparisons (34). In addition, Ranch Hands with the highest current dioxin levels were at greater risk for the development of systemic arterial hypertension than were Comparisons. In contrast, there was a significant reduction in risk for the development of heart disease reported historically or by a verified medical records review.

In the 1992 follow-up examination, Ranch Hands were more likely than Comparisons to have elevated systolic blood pressures, and through 1990, there was an increase in cardiovascular disease mortality in the nonflying enlisted personnel. However, surviving Ranch Hands overall were found to be less at risk for the development of heart disease over time, and a significant inverse dose-response effect was noted with respect to the current body burden of dioxin (35).

14.1.2 Summary of Previous Analyses of the Air Force Health Study

14.1.2.1 1982 Baseline Study Summary Results

The 1982 baseline examination found no statistically significant differences between the Ranch Hand and Comparison groups in systolic or diastolic blood pressure, the frequency of abnormal electrocardiographs (ECGs), heart sound abnormalities, abnormal funduscopic findings, or carotid bruits. A statistically significant difference emerged in the frequency of abnormal peripheral pulses: 12.8 percent of the non-Black Ranch Hands exhibited absent or diminished peripheral pulses, compared to 9.4 percent of the non-Black Original Comparisons ($p=0.05$). No statistically significant differences were found between the two groups in the occurrence of reported or verified heart disease or heart attacks.

Greater than 80 percent of the cardiac conditions reported on the study questionnaire were verified by a detailed review of medical records. There was also a strong correlation between the past medical history of cardiac disease and the baseline examination cardiovascular findings, although the differences in peripheral pulse abnormalities occurred primarily in older individuals without a history of cardiovascular

disease. Finally, the well-known risk factors of age, smoking, and cholesterol were found to be correlated with each other and with several of the cardiovascular response variables.

14.1.2.2 1985 Follow-up Study Summary Results

The analysis of cardiovascular disease history did not reveal significant group differences in reported or verified hypertension, reported heart disease, or reported or verified heart attacks. There were no group differences in verified heart disease. The verified cardiovascular history and the central and peripheral cardiovascular abnormalities detected at the physical examination were correlated, supporting accuracy and validity of the cardiovascular measurements.

In the analyses of peripheral vascular function, no significant overall group differences were observed for abnormalities involving radial, femoral, popliteal, posterior tibial, dorsalis pedis, or three anatomic aggregates of these pulses (leg pulses, peripheral pulses, and all pulses), either by manual palpation or Doppler techniques. This overall finding was in distinct contrast to the 1982 baseline examination, which, by the manual palpation method, showed significant peripheral pulse deficits in Ranch Hands. This reversal in pulse findings over the two examinations may be attributed to the rigid 4-hour tobacco abstinence applied prior to Doppler testing, although other factors may have been involved.

14.1.2.3 1987 Follow-up Study Summary Results

The assessment of the central cardiac function also found the groups to be similar, although significantly fewer Ranch Hands than Comparisons had bradycardia and more Ranch Hands than Comparisons had arrhythmias (marginally significant).

For the peripheral vascular function, Ranch Hands had a higher or marginally higher mean or percent abnormal for diastolic blood pressure (continuous form), carotid bruits, femoral pulses, and dorsalis pedis pulses than did Comparisons. No difference between the two groups was detected in the discrete analysis of diastolic blood pressure. The percentage of radial pulse abnormalities was marginally higher in Comparisons than in Ranch Hands. On the three pulse indices (leg, peripheral, and all pulses), Ranch Hands had marginally or significantly higher percentages of abnormalities than did Comparisons.

14.1.2.4 Serum Dioxin Analysis of 1987 Follow-up Study Summary Results

The cardiovascular evaluation found a marginally significant association between initial dioxin and a decrease in the reported history of heart disease, and a significant negative association with verified history of heart disease. In addition, the analyses of categorized current dioxin also indicated a decrease in verified history of heart disease for Ranch Hands with the highest current dioxin levels relative to Comparisons with background levels. These Ranch Hands also had more essential hypertension by history (after removing the variables body fat and cholesterol from the model).

The analyses of the peripheral vascular function variables displayed significantly higher mean levels of diastolic blood pressure for Ranch Hands in the low and high categories than Comparisons (without adjustment for body fat). Similar to the analysis of systolic blood pressure, the discretized analysis of diastolic blood pressure did not display a significant association with dioxin within the low and high current dioxin categories. Ranch Hands generally exhibited a significant or marginally significant higher risk of absent femoral, dorsalis pedis, and posterior tibial pulses relative to Comparisons. These observations could represent a subclinical effect and emphasize the importance of continued follow-up and evaluation.

14.1.2.5 1992 Follow-up Study Summary Results

The cardiovascular evaluation found a marginally significant group difference for verified heart disease, excluding essential hypertension for enlisted flyers with Ranch Hands having a greater history of heart disease than Comparisons. Similar to the 1987 study, verified heart disease decreased significantly for increasing levels of current dioxin. Ranch Hands also displayed an increased history of essential hypertension for increasing levels of current dioxin.

A few other central cardiac function endpoints, including non-specific ST- and T-wave changes, right bundle branch block, and prior ECG evidence of myocardial infarction, displayed significant positive associations with current dioxin; none of these endpoints also displayed any group difference between Ranch Hands and Comparisons. These findings, in conjunction with the increase in the number of deaths caused by diseases of the circulatory system for Ranch Hand nonflying enlisted personnel based on the 1994 AFHS mortality update (34), showed potential associations with dioxin requiring further observation.

The analyses of the peripheral vascular function variables displayed significant group differences for the enlisted groundcrew stratum for a few of the pulse endpoints and significant differences between Ranch Hands in the high dioxin category and Comparisons. None of these associations was reinforced by a significant association with initial or current dioxin. Longitudinal analyses of the pulse endpoints also indicated that Ranch Hands in the enlisted groundcrew stratum and in the high initial dioxin category had a greater prevalence of pulse deficits since the 1985 follow-up examination than Comparisons. Again, these associations were not reinforced by a significant dose-response effect with initial dioxin.

In general, after reviewing the results of the cardiovascular assessment as a whole, the development of cardiovascular disease did not appear to be associated positively with dioxin. Dioxin associations with selected endpoints, as discussed above, together with mortality results, pointed to the need for further evaluation.

14.1.3 Parameters for the 1997 Cardiovascular Assessment

14.1.3.1 Dependent Variables

The analysis of the cardiovascular assessment was based on data collected from the 1997 questionnaire and physical examination and subsequent medical records verification. No laboratory examination data were analyzed as cardiovascular dependent variables, although data from the laboratory examination were used as covariates.

14.1.3.1.1 Medical Records Data

During the baseline, 1985, 1987, and 1992 AFHS examination health interviews, each participant was asked whether he had a heart condition. Medical records were sought to verify all reported conditions and to determine the time of occurrence of major cardiac events. In addition, the self-reported review-of-systems recorded the overall history of heart trouble and other serious illnesses. Data collected in a similar fashion at the 1997 follow-up was verified and combined with data from the four previous examinations to create a lifetime history for four conditions: essential hypertension, heart disease (excluding essential hypertension), myocardial infarction, and stroke or transient ischemic attack. Each of these conditions was classified as "yes" or "no" and analyzed.

International Classification of Diseases, 9^{th} Revision, Clinical Modification (ICD-9-CM) codes were used to construct the four conditions described above. The following ICD-9-CM codes were used: essential hypertension (ICD-9-CM codes 401.0-401.9), heart disease (excluding essential hypertension)

(ICD-9-CM codes 391.0-391.9, 392.0, 393.0-398.99, 402.0-402.91, 404.0-404.9, 410.0-417.9, and 420.0-429.9), myocardial infarction (ICD-9-CM codes 410.0-410.9, and 412), and stroke or transient ischemic attack (ICD-9-CM codes 435.0-436).

Participants with a verified pre-SEA heart condition were excluded from all analyses. A pre-SEA heart condition included pre-SEA myocardial infarction, but did not include pre-SEA essential hypertension. Participants with a verified pre-SEA history of essential hypertension also were excluded from the analysis of verified history of essential hypertension.

14.1.3.1.2 Physical Examination Data and Self-reported Questionnaire Data

Cardiovascular data analyzed from the 1997 physical examination were divided into two main categories: central cardiac function and peripheral vascular function.

14.1.3.1.2.1 Central Cardiac Function

The assessment of the central cardiac function at the cardiovascular examination was made by measurements of systolic blood pressure, diastolic blood pressure, heart sounds (by auscultation), and an ECG. Systolic and diastolic blood pressure were determined by a Critikon Dinamap 1846SXP® automated electronic monitor with the nondominant arm placed at heart level; the lowest diastolic pressure and the corresponding systolic pressure were recorded. Detection of abnormal heart sounds was conducted by standard auscultation with the participant placed in sitting, supine, and left lateral supine positions. Fourth heart sounds were assessed; murmurs were graded in intensity and location and were judged by the examiners to be functional (normal) or organic (abnormal) in nature. The standard 12-lead ECG was performed, and an additional strip in limb lead II was produced if any arrhythmia was found. Participants were asked to abstain from tobacco for at least 4 hours prior to the ECG because of the arterial constrictive effect of nicotine. The following items were considered to be abnormal: right bundle branch block, left bundle branch block, nonspecific ST- and T-wave changes, bradycardia (a resting pulse rate less than 50 beats per minute), tachycardia (a resting pulse rate greater than 100 beats per minute), arrhythmia (any irregularity of heart rhythm including premature beats but excluding normal sinus rhythm), evidence of a prior myocardial infarction, and other diagnoses (e.g., ventricular aneurysm, Wolff-Parkinson-White syndrome). Some arrhythmias (e.g., atrial flutter, atrial fibrillation, and junctional rhythm) required more evaluation and surveillance than others, but all were grouped together for evaluation in this study.

Variables analyzed in the evaluation of the central cardiac function included systolic blood pressure, diastolic blood pressure, heart sounds, an overall ECG assessment, and eight conditions associated with the ECG. These eight conditions were right bundle branch block, left bundle branch block, nonspecific ST- and T-wave changes, bradycardia, tachycardia, arrhythmia, evidence of a prior myocardial infarction, and other diagnoses. Both systolic and diastolic blood pressure were analyzed as a continuous variable and also as a discrete variable. Systolic blood pressure was classified as "normal" (≤140 mm Hg) and "high" (>140 mm Hg), and diastolic blood pressure was classified as "normal" (≤90 mm Hg) and "high" (>90 mm Hg). Participants with a verified pre-SEA heart condition were excluded from all analyses of the central cardiac function variables.

14.1.3.1.2.2 Peripheral Vascular Function

The peripheral vascular function was assessed during the cardiovascular examination by funduscopic examination of small vessels; presence or absence of carotid bruits; determination of the radial, femoral, popliteal, dorsalis pedis, and posterior tibial pulses by Doppler techniques; and a measure of intermittent claudication and vascular insufficiency.

The funduscopic examination was conducted with undilated pupils in a standard manner, with emphasis placed upon the detection of increased light reflex, arteriovenous nicking (a sign of chronic blood pressure elevation), hemorrhages, exudates, papilledema, and arteriolar spasm. The presence or absence of carotid bruits was assessed by auscultation over both carotid arteries.

The Doppler procedure for examining pulses is a progressive array of measurements designed to determine whether a pulse abnormality exists, where the obstruction is most likely located, and whether it has functional implications. The determination of a pulse abnormality was based upon an analysis of recorded Doppler waveform morphology. Pulsatility, systolic forward flow, diastolic reverse flow, and diastolic oscillations were examined.

The funduscopic examination, carotid bruits, and the five pulses also were dichotomized as "abnormal" or "normal" (or "presence" or "absence") and analyzed. Pulses were considered abnormal if no arterial flow or a monophasic arterial flow was present on either side. In addition, two pulse indices were constructed from the radial, femoral, popliteal, dorsalis pedis, and posterior tibial pulse measurements as follows:

- Leg pulses: femoral, popliteal, dorsalis pedis, and posterior tibial pulses
- Peripheral pulses: radial, femoral, popliteal, dorsalis pedis, and posterior tibial pulses.

Each of these indices was considered "normal" if all components were normal and "abnormal" if one or more pulses were abnormal.

In the 1997 questionnaire, each participant was asked the following questions:

- Do you get a pain in either or both of your legs while walking?
- Does this pain ever begin when you are standing still or sitting?
- Do you get this pain in either or both of your calf muscles?

The self-reported answers were used to detect intermittent claudication and vascular insufficiency (yes, no), which indicate an insufficient oxygen supply to the leg muscles. A participant was judged to have intermittent claudication and vascular insufficiency if he answered "yes" to the first and third questions and "no" to the second question. Participants with a verified pre-SEA heart condition were excluded from all analyses of the peripheral vascular function variables.

14.1.3.2 Covariates

A number of covariates were examined for inclusion in the adjusted analysis of the cardiovascular assessment. Many of these covariates are considered to be classical risk factors for chronic heart disease. Covariates examined included age, race, military occupation, lifetime alcohol history, current alcohol use, lifetime cigarette smoking history, current level of cigarette smoking, cholesterol, high-density lipoprotein (HDL), cholesterol-HDL ratio, body fat, personality type, family history of heart disease, family history of heart disease before the age of 45, diabetic class, and current use of blood pressure medication (for the blood pressure variables).

Age, race, and military occupation were determined from military records. Lifetime alcohol history was based on information from the 1997 questionnaire and combined with similar information gathered at the 1987 and 1992 follow-up examinations. Each participant was asked about his drinking patterns throughout his lifetime. When a participant's drinking patterns changed, he was asked to describe how his alcohol consumption differed and the duration of time that the drinking pattern lasted. The participant's average daily alcohol consumption was determined for each of the reported drinking pattern

periods throughout his lifetime, and an estimate of the corresponding total number of drink-years was derived. One drink-year was the equivalent of drinking 1.5 ounces of an 80-proof alcoholic beverage, one 12-ounce beer, or one 5-ounce glass of wine per day for 1 year.

Current cigarette smoking and lifetime cigarette smoking history were based on questionnaire data. For lifetime cigarette smoking history, the respondent's average smoking was estimated over his lifetime based on his responses to the 1997 questionnaire, with 1 pack-year defined as 365 packs of cigarettes smoked during a single year.

Cholesterol, HDL, and the cholesterol-HDL ratio were based on 1997 laboratory measurements. Body fat was calculated from a metric body mass index (50); the formula is

$$Body\ Fat\,(in\ percent) = \frac{Weight\,(kg)}{[Height\,(m)]^2} \bullet 1.264 - 13.305.$$

Personality type was determined from the Jenkins Activity Survey administered during the 1997 follow-up examination and was derived from a discriminant-function equation based on questions that best discriminate men judged to be type A from those judged to be type B (51). Positive scores reflected the type A direction and negative scores reflected the type B direction. Personality type was dichotomized as type A or type B.

Family history of heart disease was defined as "yes" if the participant's mother, father, sister(s), or brother(s) had heart trouble or heart disease and "no" otherwise. Family history of heart disease before the age of 45 was defined as "yes" if the participant's mother, father, sister(s), or brother(s) had heart trouble or heart disease before the age of 45 and "no" otherwise. Blood pressure medication (yes, no) was used as a covariate for the adjusted analysis of the systolic and diastolic blood pressure variables only.

Diabetic class was used as a covariate in the analysis of the 1997 follow-up. Diabetes is a known risk factor for cardiovascular disease. In the 1997 questionnaire, a general screening question on diabetes was posed. Each participant was asked during the in-person health interview the following question: "Since the date of the last interview, has a doctor told you for the first time that you had diabetes?" All affirmative responses were verified by a medical records review and added to previously reported and verified information on diabetes from the 1982 baseline and the 1985, 1987, and 1992 follow-up examinations for each participant. Participants with a verified history of diabetes were combined with those participants with a 2-hour postprandial glucose level of 200 mg/dl or greater at the 1997 physical examination and classified as "diabetic" for the diabetic class covariate. Those participants without a verified history of diabetes and with a 2-hour postprandial glucose level of less than 200 mg/dl at the 1997 physical examination were classified as either "impaired" (140 mg/dl $\leq$ 2-hour postprandial glucose $<$ 200 mg/dl) or "normal" (2-hour postprandial glucose $<$ 140 mg/dl).

The current use of blood pressure medication was used as a covariate for the adjusted analysis of systolic and diastolic blood pressures. This information was reported by the participant on a self-reported form that listed physicians and medications, and through a question in the in-person interview.

The following dependent variables—essential hypertension, heart disease excluding essential hypertension, myocardial infarction, and stroke or transient ischemic attack—capture a history of a cardiovascular condition rather than the current state of a participant's life at the time of the physical examination. Consequently, to reflect the historical nature of these dependent variables, lifetime alcohol history and lifetime cigarette smoking history were used as covariates, but current alcohol use and current cigarette smoking were not. Lifetime alcohol history and lifetime cigarette smoking history reflect the

cumulative lifetime effects of alcohol use and tobacco, respectively, whereas current alcohol use and current cigarette smoking emphasize the short period of time near the date of the physical examination.

14.1.4 Statistical Methods

Table 14-1 summarizes the statistical analysis performed for the cardiovascular assessment. The first part of this table describes the dependent variables and identifies the covariates and the statistical methods. The second part of this table further describes the covariates. A covariate was used in its continuous form whenever possible for all adjusted analyses. If a covariate was inherently discrete (e.g., military occupation), or if a categorized form was needed to develop measures of association with the dependent variables, the covariate was categorized as shown in Table 14-1.

Table 14-2 provides a summary of the number of participants with missing dependent variable or covariate data. In addition, the number of participants excluded from analysis is given.

Table 14-1. Statistical Analysis for the Cardiovascular Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
Essential Hypertension	MR-V	D	Yes No	(1)	(a)	U:LR A:LR
Heart Disease (Excluding Essential Hypertension)	MR-V	D	Yes No	(1)	(b)	U:LR A:LR
Myocardial Infarction	MR-V	D	Yes No	(1)	(b)	U:LR A:LR
Stroke or Transient Ischemic Attack	MR-V	D	Yes No	(1)	(b)	U:LR,CS A:LR
Systolic Blood Pressure (mm Hg)	PE	D/C	High: >140 Normal: ≤140	(2)	(b)	U:LR,GLM A:LR,GLM L:LR,GLM
Diastolic Blood Pressure (mm Hg)	PE	D/C	High: >90 Normal: ≤90	(2)	(b)	U:LR,GLM A:LR,GLM
Heart Sounds	PE	D	Abnormal Normal	(3)	(b)	U:LR A:LR
Overall Electrocardiograph (ECG)	PE	D	Abnormal Normal	(3)	(b)	U:LR A:LR
ECG: Right Bundle Branch Block	PE	D	Yes No	(3)	(b)	U:LR A:LR
ECG: Left Bundle Branch Block	PE	D	Yes No	(3)	(b)	U:LR,CS A:LR
ECG: Non-specific ST-and T-Wave Changes	PE	D	Yes No	(3)	(b)	U:LR A:LR
ECG: Bradycardia	PE	D	Yes No	(3)	(b)	U:LR A:LR
ECG: Tachycardia	PE	D	Yes No	(3)	(b)	U:LR,CS A:LR

Table 14-1. Statistical Analysis for the Cardiovascular Assessment (Continued)

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
ECG: Arrhythmia	PE	D	Yes No	(3)	(b)	U:LR A:LR
ECG: Evidence of Prior Myocardial Infarction	PE	D	Yes No	(3)	(b)	U:LR A:LR
ECG: Other Diagnoses	PE	D	Yes No	(3)	(b)	U:LR,CS A:LR
Funduscopic Examination	PE	D	Abnormal Normal	(3)	(b)	U:LR A:LR
Carotid Bruits	PE	D	Present Absent	(3)	(b)	U:LR A:LR
Radial Pulses	PE	D	Abnormal Normal	(3)	(b)	U:LR A:LR
Femoral Pulses	PE	D	Abnormal Normal	(3)	(b)	U:LR A:LR L:LR
Popliteal Pulses	PE	D	Abnormal Normal	(3)	(b)	U:LR A:LR L:LR
Dorsalis Pedis Pulses	PE	D	Abnormal Normal	(3)	(b)	U:LR A:LR L:LR
Posterior Tibial Pulses	PE	D	Abnormal Normal	(3)	(b)	U:LR A:LR L:LR
Leg Pulses	PE	D	Abnormal Normal	(3)	(b)	U:LR A:LR L:LR
Peripheral Pulses	PE	D	Abnormal Normal	(3)	(b)	U:LR A:LR L:LR
Intermittent Claudication and Vascular Insufficiency (ICVI) Index	Q-SR	D	Abnormal Normal	(3)	(b)	U:LR A:LR

[a]Covariates:
(1): age, race, military occupation, lifetime cigarette smoking history, lifetime alcohol history, cholesterol, HDL, cholesterol-HDL ratio, diabetic class, body fat, personality type, family history of heart disease, family history of heart disease before age 45.
(2): age, race, military occupation, lifetime cigarette smoking history, current cigarette smoking, lifetime alcohol history, current alcohol use, cholesterol, HDL, cholesterol-HDL ratio, diabetic class, body fat, personality type, family history of heart disease, family history of heart disease before age 45, taking blood pressure medication.
(3): age, race, military occupation, lifetime cigarette smoking history, current cigarette smoking, lifetime alcohol history, current alcohol use, cholesterol, HDL, cholesterol-HDL ratio, diabetic class, body fat, personality type, family history of heart disease, family history of heart disease before age 45.

[b]Exclusions:
(a): participants with a pre-SEA heart condition, participants with pre-SEA essential hypertension.
(b): participants with a pre-SEA heart condition.

Table 14-1. Statistical Analysis for the Cardiovascular Assessment (Continued)

Covariates

Variable (Units)	Data Source	Data Form	Cutpoints
Age (years)	MIL	D/C	Born ≥1942 Born <1942
Race	MIL	D	Black Non-Black
Occupation	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Lifetime Alcohol History (drink-years)	Q-SR	D/C	0 >0–40 >40
Current Alcohol Use (drinks/day)	Q-SR	D/C	0–1 >1–4 >4
Lifetime Cigarette Smoking History (pack-years)	Q-SR	D/C	0 >0–10 >10
Current Cigarette Smoking (cigarettes/day)	Q-SR	D/C	0-Never 0-Former >0–20 >20
Cholesterol (mg/dl)	LAB	D/C	≤200 >200–239 >239
High Density Lipoprotein (mg/dl)	LAB	D/C	0–35 >35
Cholesterol-HDL Ratio	LAB	D/C	0–5 >5
Body Fat (percent)	PE	D/C	Obese: >25% Lean or Normal: ≤25%
Personality Type	PE	D	A direction B direction
Family History of Heart Disease	Q-SR	D	Yes No
Family History of Heart Disease Before Age 45	Q-SR	D	Yes No
Diabetic Class	LAB/MR-V	D	• Diabetic: past history or ≥200 mg/dl 2-hr. postprandial glucose • Impaired: 140–<200 mg/dl 2-hr. postprandial glucose • Normal: <140 mg/dl 2-hr. postprandial glucose
Taking Blood Pressure Medication	Q-SR/MR-V	D	Yes No

Table 14-1. Statistical Analysis for the Cardiovascular Assessment (Continued)

Abbreviations

Data Source: LAB: 1997 laboratory results
MIL: Air Force military records
MR-V: Medical records (verified)
PE: 1997 physical examination
Q-SR: Health questionnaires (self-reported)

Data Form: D: Discrete analysis only
D/C: Discrete and continuous analyses for dependent variables; appropriate form for analysis (either discrete or continuous) for covariates

Statistical Analysis: U: Unadjusted analysis
A: Adjusted analysis
L: Longitudinal analysis

Statistical Methods: CS: Chi-square contingency table analysis (continuity-adjusted)
GLM: General linear models analysis
LR: Logistic regression analysis

Table 14-2. Number of Participants Excluded or with Missing Data for the Cardiovascular Assessment

Variable	Variable Use	Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
		Ranch Hand	Comparison	Initial	1987	Ranch Hand	Comparison
Funduscopic Examination	DEP	1	1	0	1	1	1
Femoral Pulses	DEP	0	1	0	0	0	1
Popliteal Pulses	DEP	0	2	0	0	0	2
Dorsalis Pedis Pulses	DEP	0	2	0	0	0	2
Posterior Tibial Pulses	DEP	0	4	0	0	0	4
Leg Pulses	DEP	0	4	0	0	0	4
Peripheral Pulses	DEP	0	4	0	0	0	4
Intermittent Claudication and Insufficiency Index	DEP	1	0	0	1	1	0
Lifetime Alcohol History	COV	6	2	3	6	6	1
Current Alcohol Use	COV	1	0	0	1	1	0
Lifetime Cigarette Smoking History	COV	2	1	1	2	2	1
Current Cigarette Smoking	COV	1	0	0	1	1	0
HDL Cholesterol	COV	1	1	1	1	1	1
Cholesterol-HDL Ratio	COV	1	1	1	1	1	1
Personality Type	COV	3	0	1	3	3	0
Family History of Heart Disease	COV	10	6	5	10	10	6
Family History of Heart Disease Before Age 45	COV	22	22	11	22	22	21
Diabetic Class	EXC	9	18	5	7	7	17

Table 14-2. Number of Participants Excluded or with Missing Data for the Cardiovascular Assessment (Continued)

Variable	Variable Use	Group: Ranch Hand	Group: Comparison	Dioxin (Ranch Hands Only): Initial	Dioxin (Ranch Hands Only): 1987	Categorized Dioxin: Ranch Hand	Categorized Dioxin: Comparison
Pre-SEA Heart Condition	EXC	11	19	6	11	11	18
Pre-SEA Essential Hypertension	EXC	11	14	7	11	11	14

Note: DEP = Dependent variable.
COV = Covariate.
EXC = Exclusion.
870 Ranch Hands and 1,251 Comparisons.
482 Ranch Hands for initial dioxin; 863 Ranch Hands for 1987 dioxin.
863 Ranch Hands and 1,213 Comparisons for categorized dioxin.

14.1.4.1 Longitudinal Analysis

The cardiovascular longitudinal analysis was based on the association of exposure with changes in systolic blood pressure between the 1982 and 1997 examinations and six pulse measurements between the 1985 and 1997 examinations. The longitudinal analysis for systolic blood pressure was based on this variable in both the continuous and discrete forms. The six pulse measurements included femoral pulses, popliteal pulses, dorsalis pedis pulses, posterior tibial pulses, leg pulses, and peripheral pulses. The 1985 and 1997 measurements were used for the pulse assessments because the Doppler assessment of pulses was conducted at these two examinations and was not conducted at the 1982 baseline examination.

14.2 RESULTS

14.2.1 Dependent Variable-Covariate Associations

The associations between the dependent variables examined in the cardiovascular assessment and the covariates used in the adjusted analysis were investigated; the results are presented in Appendix F, Table F-6. These associations are pairwise between the dependent variable and the covariate and are not adjusted for any other covariates. Participants with a pre-SEA heart condition were excluded from all analyses. In addition, participants with pre-SEA essential hypertension were excluded from the analysis of essential hypertension.

Tests of covariate association showed age (p=0.001), lifetime alcohol history (p=0.001), cholesterol-HDL ratio (p=0.005), body fat (p=0.001), personality type (p=0.039), family history of heart disease (p=0.001), family history of heart disease before age 45 (p=0.003), and diabetic class (p=0.001) to be significantly associated with essential hypertension. Older participants had more essential hypertension than did younger participants (48.0% versus 32.9%). Essential hypertension was highest for the heaviest drinkers (in terms of drink-years) (48.2%), followed by participants who did not drink (39.0%), then moderate drinkers (38.5%). Essential hypertension increased with the cholesterol-HDL ratio and body fat. Participants with personality type B had a higher percentage of essential hypertension than did type A participants (43.0% versus 38.4%). Essential hypertension occurred more often for participants who had a family history of heart disease and for participants who had a family history of heart disease before age 45. Essential hypertension was greatest for diabetics (59.4%), followed by participants in the impaired diabetic class (52.4%), then participants classified as normal (34.6%).

Heart disease (excluding essential hypertension) was significantly associated with age (p=0.001), occupation (p=0.001), cholesterol (p=0.001), family history of heart disease (p=0.001), family history of heart disease before age 45 (p=0.018), and diabetic class (p=0.009). Heart disease increased with age and decreased with cholesterol level. Officers had the highest percentage of heart disease (68.7%), followed by enlisted flyers (66.6%), then enlisted groundcrew (56.7%). Participants with a family history of heart disease had more heart disease (66.6% versus 57.4%). Likewise, participants with a family history of heart disease before age 45 had more heart disease (69.9% versus 62.0%). Diabetic participants had the most heart disease (69.5%), followed by participants in the impaired diabetic class (64.1%), then participants classified as normal (60.8%).

The percentage of participants with a history of a myocardial infarction increased significantly with age (p=0.001) and lifetime cigarette smoking history (p=0.001), while decreasing significantly with cholesterol (p=0.001) and HDL cholesterol (p=0.012). The association with diabetic class was also significant (p=0.001). Participants in the normal diabetic class had the lowest percentage of participants with a myocardial infarction (6.8%), followed by participants in the impaired diabetic class (9.9%), then diabetics (14.2%).

Systolic blood pressure in its continuous form increased with age (p<0.001), lifetime alcohol history (p<0.001), lifetime cigarette smoking history (p=0.045), cholesterol (p=0.012), the cholesterol-HDL ratio (p=0.005), and body fat (p<0.001). Systolic blood pressure decreased significantly with current cigarette smoking (p=0.004). Tests of covariate associations also showed significant relations with occupation (p=0.005), diabetic class (p<0.001), and blood pressure medication (p<0.001). Enlisted flyers had the highest mean systolic blood pressure levels (127.1 mm Hg), followed by officers (126.1 mm Hg), then enlisted groundcrew (123.9 mm Hg). Participants in the normal diabetic class had the lowest mean systolic blood pressure levels (123.0 mm Hg), followed by participants in the impaired diabetic class (129.3 mm Hg), then diabetic participants (131.8 mm Hg). Participants taking blood pressure medication had a higher mean systolic blood pressure level (128.6 mm Hg) than those not taking blood pressure medication (123.9 mm Hg).

Systolic blood pressure in its dichotomous form increased with age (p=0.001), cholesterol (p=0.025), the cholesterol-HDL ratio (p=0.028), and body fat (p=0.001). Significant associations also were seen between systolic blood pressure and occupation (p=0.029), family history of heart disease (p=0.008), diabetic class (p=0.001), and blood pressure medication (p=0.001). Enlisted flyers had the greatest percentage of high systolic blood pressure values (23.6%), followed by officers (23.2%), then enlisted groundcrew (18.6%). Participants with a family history of heart disease had a greater prevalence of high systolic blood pressure values than did participants with no history of heart disease (23.3% versus 18.3%). Diabetic participants had the largest percentage of high systolic blood pressure values (31.9%), followed by participants in the impaired diabetic class (28.6%), then participants classified as normal (17.1%). Participants taking blood pressure medication had a greater prevalence of high systolic blood pressure values than participants not taking blood pressure medication (27.6% versus 18.5%).

Diastolic blood pressure in its continuous form decreased with age (p=0.009), lifetime cigarette smoking history (p=0.003), and current cigarette smoking (p=0.001). Diastolic blood pressure increased with cholesterol (p<0.001), the cholesterol-HDL ratio (p=0.004), and body fat (p<0.001). Race and diabetic class were also significantly associated with diastolic blood pressure (p=0.010 and p=0.030, respectively). Black participants had a higher mean diastolic blood pressure than non-Black participants (76.69 mm Hg versus 74.46 mm Hg). Participants in the impaired diabetic class had the highest mean diastolic blood pressure (75.94 mm Hg), followed by diabetic participants (74.41 mm Hg), then participants classified as normal (74.32 mm Hg).

Tests of covariate association for diastolic blood pressure in its discrete form showed significant relations with lifetime cigarette smoking history (p=0.003) and blood pressure medication (p=0.004). Moderate lifetime cigarette smokers (in terms of pack-years) had the greatest percentage of high diastolic blood pressure values (7.8%), followed by participants who never smoked and participants who were the heaviest smokers (4.1% each). Participants taking blood pressure medication had a greater prevalence of high diastolic blood pressure values than did participants not taking blood pressure medication (7.3% versus 4.1%).

The percentage of participants with abnormal heart sounds increased with age (p=0.001). Current cigarette smoking was also significantly associated with heart sounds (p=0.030). Former smokers had the highest prevalence of abnormal heart sounds (5.7%), followed by participants who smoked up to 20 cigarettes per day (3.4%), participants who smoked more than 20 cigarettes per day (2.9%), and participants who never smoked (2.9%).

The prevalence of abnormal overall ECG results increased with age (p=0.001) and body fat (p=0.008), while decreasing with cholesterol (p=0.041). Also significant were occupation (p=0.001), lifetime cigarette smoking history (p=0.002), current cigarette smoking (p=0.028), personality type (p=0.011), family history of heart disease (p=0.001), and diabetic class (p=0.001). Enlisted flyers had the highest percentage of abnormal overall ECG results (36.4%), followed by officers (34.6%), then enlisted groundcrew (26.3%). Heavy lifetime cigarette smokers (in terms of pack-years) had the highest percentage of abnormal overall ECG results (35.0%), followed by participants who never smoked (28.3%), then moderate lifetime cigarette smokers (27.6%). Participants who currently smoked up to 20 cigarettes per day had the highest percentage of abnormal overall ECG results (35.0%), followed by former smokers (32.8%), participants who never smoked (28.3%), and participants who smoked more than 20 cigarettes per day (23.5%). Participants with type B personalities had a higher percentage of abnormal overall ECG results (33.2%) than did participants with type A personalities (27.8%). Participants with a family history of heart disease had a higher prevalence of abnormal overall ECG results than did participants with no family history of heart disease (35.3% versus 24.6%). Diabetic participants had the highest percentage of abnormal overall ECG results (46.7%), followed by participants in the impaired diabetic class (37.0%), then participants classified as normal (26.4%).

The prevalence of right bundle branch block increased significantly with age (p=0.001). Also significantly associated with right bundle branch block were occupation (p=0.040), lifetime cigarette smoking history (p=0.048), and diabetic class (p=0.001). Enlisted flyers had the highest prevalence of right bundle branch block (4.5%), followed by officers (2.6%), then enlisted groundcrew (1.9%). Heavy lifetime cigarette smokers had the highest prevalence of right bundle branch block (3.5%), followed by nonsmokers (2.2%), then moderate lifetime smokers (1.5%). Diabetic participants had the highest percentage of right bundle branch block (5.4%), followed by participants in the impaired diabetic class (2.6%), then participants classified as normal (1.9%).

The percentage of non-specific ST- and T-wave changes increased with age (p=0.001) and body fat (p=0.001), while decreasing with lifetime alcohol use (p=0.024). Family history of heart disease (p=0.001) and diabetic class (p=0.001) also were significant. Participants with a family history of heart disease had a higher percentage of non-specific ST- and T-wave changes than did participants with no history (21.1% versus 14.0%). Diabetic participants had the highest prevalence of non-specific ST- and T-wave changes (29.3%), followed by participants in the impaired diabetic class (24.5%), then participants classified as normal (14.6%).

The prevalence of bradycardia increased significantly with HDL cholesterol levels (p=0.043), while decreasing with the cholesterol-HDL ratio (p=0.005) and body fat (p=0.001). Occupation and diabetic

class also were significantly related to bradycardia (p=0.001 each). Officers had the highest prevalence of bradycardia (5.6%), followed by enlisted flyers (3.0%), then enlisted groundcrew (1.8%). Participants in the normal diabetic class had the highest prevalence of bradycardia (4.5%), followed by diabetic participants (1.7%), then participants in the impaired diabetic class (0.4%).

Tachycardia was significantly associated with lifetime alcohol history (p=0.029) and diabetic class (p=0.008). Non-drinkers had the highest prevalence of tachycardia (1.7%), followed by heavy drinkers (0.8%), then moderate lifetime alcohol drinkers (0.2%). Diabetic participants had the highest prevalence of tachycardia (1.4%), followed by participants in the impaired diabetic class (0.4%), then participants classified as normal (0.2%).

The percentage of participants with arrhythmia increased with age (p=0.001).

Evidence of prior myocardial infarction from the ECG increased with age (p=0.001) and decreased with cholesterol levels (p=0.007). Lifetime cigarette smoking history (p=0.003) and diabetic class (p=0.001) also were significantly associated with prior myocardial infarction. Heavy lifetime cigarette smokers had the highest prevalence of a prior myocardial infarction (5.8%), followed by nonsmokers (2.9%), then moderate lifetime cigarette smokers (2.7%). Diabetic participants had the highest percentage of participants with evidence of a prior myocardial infarction (9.4%), followed by participants in the impaired diabetic class (5.1%), then participants classified as normal (2.8%).

The prevalence of abnormal funduscopic examination results increased with age (p=0.001), lifetime cigarette smoking history (p=0.001), and body fat (p=0.004). Occupation (p=0.001), current cigarette smoking (p=0.019), personality type (p=0.001), and diabetic class (p=0.001) were also significantly associated with an abnormal funduscopic examination. Enlisted flyers had the highest percentage of abnormal funduscopic examination results (18.6%), followed by enlisted groundcrew (11.5%), then officers (11.1%). Participants who never smoked had the lowest percentage of abnormal funduscopic exam results (8.9%), followed by participants who currently smoked up to 20 cigarettes per day (13.5%), former smokers (14.0%), and participants who currently smoked more than 20 cigarettes per day (14.1%). Abnormal funduscopic examinations were more prevalent for participants with personality type B than those with personality type A (14.4% versus 9.2%). Diabetic participants had the highest percentage of abnormal funduscopic exam results (20.0%), followed by participants in the impaired diabetic class (14.3%), then participants classified as normal (10.3%).

The percentage of participants with carotid bruits present increased with age (p=0.001) and lifetime cigarette smoking history (p=0.003). Current cigarette smoking and diabetic class also were significantly associated with carotid bruits (p=0.023 and p=0.007, respectively). Participants who currently smoked up to 20 cigarettes per day had the highest percentage of carotid bruits present (4.1%), followed by participants who currently smoked more than 20 cigarettes per day (3.7%), former smokers (3.1%), and participants who never smoked (1.0%). Diabetic participants had the highest prevalence of carotid bruits (5.1%), followed by participants in the impaired diabetic class (2.9%), then participants classified as normal (2.1%).

Tests of covariate association showed race (p=0.018), lifetime alcohol history (p=0.006), current alcohol use (p=0.005), and current cigarette smoking (p=0.010) to be significantly associated with abnormal radial pulses. The prevalence of abnormal results increased with lifetime alcohol use. Black participants had a higher percentage of abnormal radial pulses than non-Blacks (2.4% versus 0.4%). Participants who currently were moderate drinkers (in terms of drinks per day) had the highest percentage of abnormal radial pulses (1.6%), followed by light drinkers (0.3%), then participants who were the heaviest drinkers (0.0%). Participants who currently smoked up to 20 cigarettes per day had the highest percentage of

abnormal radial pulses (1.9%), followed by participants who currently smoked more than 20 cigarettes per day (0.7%), former smokers (0.4%), and participants who never smoked (0.2%).

The prevalence of abnormal femoral pulses increased with age (p=0.009), lifetime alcohol history (p=0.002), and lifetime cigarette smoking history (p=0.002). Also significant were current alcohol use (p=0.001), current cigarette smoking (p=0.001), and diabetic class (p=0.003). Participants who were currently moderate drinkers had the highest percentage of abnormal femoral pulses (4.4%), followed by the heaviest drinkers (4.0%), then the light drinkers (1.0%). Participants who currently smoked up to 20 cigarettes per day had the highest percentage of abnormal femoral pulses (4.9%), followed by participants who currently smoked more than 20 cigarettes per day (4.4%), former smokers (1.2%), and participants who never smoked (0.3%). Diabetic participants had the highest percentage of abnormal femoral pulses (3.7%), followed by participants classified as normal (1.2%), then participants in the impaired diabetic class (1.1%).

The percentage of participants with abnormal popliteal pulses increased with age (p=0.001), lifetime alcohol history (p=0.013), current alcohol use (p=0.002), lifetime cigarette smoking history (p=0.001), and current cigarette smoking (p=0.001). The association with diabetic class also was significant (p=0.001). Participants who were currently moderate drinkers had the highest percentage of abnormal popliteal pulses (4.9%), followed by the heaviest drinkers (4.0%), then participants who were the lightest drinkers (1.9%). Participants who currently smoked up to 20 cigarettes per day had the highest percentage of abnormal popliteal pulses (7.1%), followed by participants who currently smoked more than 20 cigarettes per day (5.1%), former smokers (2.0%), and participants who never smoked (0.5%). Diabetic participants had the highest percentage of abnormal popliteal pulses (6.0%), followed by participants in the impaired diabetic class (1.8%), then participants classified as normal (1.7%).

The prevalence of abnormal dorsalis pedis pulses increased with age (p=0.001), lifetime cigarette smoking history (p=0.001), and current cigarette smoking (p=0.001). Lifetime alcohol history and diabetic class also were significant (p=0.009 and p=0.001, respectively). Heavy lifetime alcohol drinkers had the highest percentage of abnormal dorsalis pedis pulses (10.6%), followed by non-drinkers (8.5%), then moderate lifetime alcohol drinkers (6.6%). Diabetic participants had the highest prevalence of abnormal dorsalis pedis pulses (14.0%), followed by participants classified as normal (6.7%), then participants in the impaired diabetic class (5.5%).

The percentage of abnormal posterior tibial pulses increased with age (p=0.001), lifetime alcohol history (p=0.027), current alcohol use (p=0.003), lifetime cigarette smoking history (p=0.001), and current cigarette smoking (p=0.001). Personality type and diabetic class also were significantly associated with posterior tibial pulses (p=0.020 and p=0.001, respectively). Participants with type B personalities had more abnormal posterior tibial pulses than participants with type A personalities (6.7% versus 4.2%). Diabetic participants had the highest prevalence of abnormal posterior tibial pulses (13.4%), followed by participants in the impaired diabetic class (5.5%), then participants classified as normal (4.1%).

Abnormal leg pulses increased with age (p=0.001), lifetime cigarette smoking history (p=0.001), and current cigarette smoking (p=0.001). Occupation (p=0.044), lifetime alcohol history (p=0.013), and personality type (p=0.012) also were associated significantly with leg pulses. Enlisted flyers had the highest percentage of abnormal leg pulses (14.2%), followed by enlisted groundcrew (10.0%), then officers (9.3%). Heavy lifetime alcohol drinkers had the highest percentage of abnormal leg pulses (13.4%), followed by non-drinkers (11.0%), then moderate lifetime alcohol drinkers (9.0%). Participants with type B personalities had more abnormal leg pulses than participants with type A personalities (11.7% versus 8.2%). Diabetic participants had the highest prevalence of abnormal leg pulses (18.8%),

followed by participants classified as normal (8.7%), then participants in the impaired diabetic class (8.4%).

The prevalence of abnormal peripheral pulses increased with age (p=0.001), lifetime cigarette smoking history (p=0.001), and current cigarette smoking (p=0.001), while decreasing with body fat (p=0.034). Lifetime alcohol history (p=0.005), current alcohol use (p=0.036), personality type (p=0.026), and diabetic class (p=0.001) also were associated significantly with abnormal peripheral pulses. Heavy lifetime alcohol drinkers had the highest percentage of abnormal peripheral pulses (14.0%), followed by non-drinkers (11.0%) and moderate lifetime alcohol drinkers (9.1%). Participants who were currently moderate drinkers had the highest percentage of abnormal peripheral pulses (14.2%), followed by the heaviest drinkers (14.0%), then participants who were the lightest drinkers (9.8%). Participants with type B personalities had a higher percentage of abnormal peripheral pulses than did participants with type A personalities (11.8% versus 8.7%). Diabetic participants had the highest prevalence of abnormal peripheral pulses (19.4%), followed by participants classified as normal (8.9%), then participants in the impaired diabetic class (8.4%).

The percentage of abnormal intermittent claudication and vascular insufficiency index (ICVI) results increased with lifetime cigarette smoking (p=0.001) and current cigarette smoking (p=0.001). Diabetic class was also significant (p=0.001). Diabetic participants had the highest percentage of abnormal ICVI results (9.1%), followed by participants in the impaired diabetic class (2.9%), then participants classified as normal (2.6%).

14.2.2 Exposure Analysis

The following section presents results of the statistical analysis of the dependent variables shown in Table 14-1. Dependent variables were derived from a medical records review and verification, physical examination and ECG determinations, and an ICVI index based on participant responses to three questions regarding leg pain.

Four models were examined for each dependent variable given in Table 14-1. The analyses of these models are presented below. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7, respectively. These analyses were performed both unadjusted and adjusted for relevant covariates. Model 1 examined the relation between the dependent variable and group (i.e., Ranch Hand or Comparison). In this model, exposure was defined as "yes" for Ranch Hands and "no" for Comparisons without regard to the magnitude of the exposure. As an attempt to quantify exposure, three contrasts of Ranch Hands and Comparisons were performed along with the overall Ranch Hand versus Comparison contrast. These three contrasts compared Ranch Hands and Comparisons within each occupational category (i.e., officers, enlisted flyers, and enlisted groundcrew). As described in previous reports and Table 2-8, the average levels of exposure to dioxin were highest for enlisted groundcrew, followed by enlisted flyers, then officers.

Model 2 explored the relation between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt. If a participant did not have a 1987 dioxin level, the 1992 level was used to estimate the initial dioxin level. If a participant did not have a 1987 or a 1992 dioxin level, the 1997 level was used to estimate the initial dioxin level. A statistical adjustment for the percentage of body fat at the time of the participant's blood measurement of dioxin was included in this model to account for body-fat-related differences in elimination rate (52).

Model 3 divided the Ranch Hands examined in Model 2 into two categories based on their initial dioxin measures. These two categories are referred to as "low Ranch Hand" and "high Ranch Hand." Two

additional categories, Ranch Hands with 1987 serum dioxin levels at or below 10 ppt and Comparisons with 1987 serum dioxin levels at or below 10 ppt, were formed and included in the model. Ranch Hands with 1987 serum dioxin levels at or below 10 ppt are referred to as the "background Ranch Hand" category. Dioxin levels in 1992 were used if the 1987 level was not available, and dioxin levels in 1997 were used if the 1987 and 1992 levels were not available. These four categories—Comparisons, background Ranch Hands, low Ranch Hands, and high Ranch Hands—were used in Model 3 analyses. The relation between the dependent variable in each of the three Ranch Hand categories and the dependent variable in the Comparison category was examined. A fourth contrast, exploring the relation of the dependent variable in the combined low and high Ranch Hand categories relative to Comparisons, also was conducted. This combination is referred to in the tables as the "low plus high Ranch Hand" category. As in Model 2, a statistical adjustment for the percentage of body fat at the time of the participant's blood measurement of dioxin was included in this model.

Model 4 examined the relation between the dependent variable and 1987 lipid-adjusted dioxin levels in all Ranch Hands with a dioxin measurement. If a participant did not have a 1987 dioxin measurement, the 1992 measurement was used to determine the dioxin level. If a participant did not have a 1987 or a 1992 dioxin measurement, the 1997 measurement was used to determine the dioxin level.

14.2.2.1 Medical Records Variables

14.2.2.1.1 Essential Hypertension

All Model 1, 2, and 3 analyses of essential hypertension revealed no significant results (Table 14-3(a–f): p>0.13 for each analysis).

The unadjusted and adjusted Model 4 analyses each showed significant positive associations between essential hypertension and 1987 dioxin (Table 14-3(g,h): Est. RR=1.22, p<0.001; Adj. RR=1.18, p=0.011). The percentages of participants with essential hypertension in the low, medium, and high 1987 dioxin categories were 34.0, 38.0, and 49.1, respectively.

Table 14-3. Analysis of Essential Hypertension

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	**Group**	**n**	**Number (%) Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***850***	***345 (40.6)***	***0.95 (0.80,1.14)***	***0.606***
	Comparison	***1,220***	***509 (41.7)***		
Officer	Ranch Hand	329	128 (38.9)	0.90 (0.68,1.20)	0.467
	Comparison	480	199 (41.5)		
Enlisted Flyer	Ranch Hand	149	71 (47.7)	1.18 (0.77,1.83)	0.447
	Comparison	184	80 (43.5)		
Enlisted Groundcrew	Ranch Hand	372	146 (39.2)	0.92 (0.70,1.20)	0.519
	Comparison	556	230 (41.4)		

Table 14-3. Analysis of Essential Hypertension (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	*0.96 (0.79,1.17)*	*0.708*
Officer	0.85 (0.63,1.16)	0.317
Enlisted Flyer	1.27 (0.79,2.04)	0.316
Enlisted Groundcrew	0.96 (0.72,1.29)	0.811

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	152	65 (42.8)	1.06 (0.91,1.23)	0.441
Medium	160	72 (45.0)		
High	159	77 (48.4)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
452	1.10 (0.91,1.32)	0.314

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,183	490 (41.4)		
Background RH	372	127 (34.1)	0.86 (0.67,1.11)	0.246
Low RH	229	94 (41.0)	0.95 (0.71,1.29)	0.758
High RH	242	120 (49.6)	1.22 (0.91,1.63)	0.177
Low plus High RH	471	214 (45.4)	1.08 (0.87,1.35)	0.488

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 14-3. Analysis of Essential Hypertension (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Comparison	1,145		
Background RH	356	0.87 (0.66,1.14)	0.320
Low RH	217	0.87 (0.63,1.20)	0.395
High RH	235	1.27 (0.93,1.74)	0.131
Low plus High RH	452	1.06 (0.84,1.35)	0.624

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**	
1987 Dioxin	**n**	**Number (%) Yes**	**Estimated Relative Risk (95% C.I.)[a]**	**p-Value**
Low	282	96 (34.0)	1.22 (1.11,1.34)	<0.001
Medium	276	105 (38.0)		
High	285	140 (49.1)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
808	1.18 (1.04,1.34)	0.011

[a] Relative risk for a twofold increase in 1987 dioxin.

14.2.2.1.2 Heart Disease (Excluding Essential Hypertension)

The unadjusted and adjusted Model 1 analyses of a history of heart disease each showed significant group differences when combining all occupations (Table 14-4(a,b): Est. RR=1.26, p=0.013; Adj. RR=1.26, p=0.018, respectively). The percentage of Ranch Hands with heart disease was 66.1 versus 60.8 percent for Comparisons. Stratifying by occupation, unadjusted and adjusted analyses revealed group differences within the enlisted flyer stratum (Table 14-4(a,b): Est. RR=2.10, p=0.003; Adj. RR=2.05; p=0.004, respectively). The percentage of Ranch Hand enlisted flyers with heart disease was 75.2 versus 59.7 percent for the Comparison enlisted flyers.

Table 14-4. Analysis of Heart Disease (Excluding Essential Hypertension)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***568 (66.1)***	***1.26 (1.05,1.51)***	***0.013***
	Comparison	***1,232***	***749 (60.8)***		
Officer	Ranch Hand	334	238 (71.3)	1.22 (0.90,1.66)	0.191
	Comparison	484	324 (66.9)		
Enlisted Flyer	Ranch Hand	149	112 (75.2)	2.10 (1.27,3.28)	0.003
	Comparison	186	111 (59.7)		
Enlisted Groundcrew	Ranch Hand	376	218 (58.0)	1.10 (0.84,1.42)	0.523
	Comparison	562	314 (55.9)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.26 (1.04,1.53)***	***0.018***
Officer	1.21 (0.88,1.66)	0.238
Enlisted Flyer	2.10 (1.28,3.45)	0.004
Enlisted Groundcrew	1.10 (0.83,1.46)	0.496

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	155	115 (74.2)	0.79 (0.68,0.91)	0.001
Medium	161	99 (61.5)		
High	160	88 (55.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
457	0.90 (0.75,1.08)	0.249

[a] Relative risk for a twofold increase in initial dioxin.

Table 14-4. Analysis of Heart Disease (Excluding Essential Hypertension) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	**n**	**Number (%) Yes**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,195	730 (61.1)		
Background RH	376	259 (68.9)	1.43 (1.11,1.83)	0.005
Low RH	233	163 (70.0)	1.48 (1.09,2.00)	0.011
High RH	243	139 (57.2)	0.84 (0.64,1.11)	0.228
Low plus High RH	476	302 (63.4)	1.11 (0.89,1.39)	0.359

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Comparison	1,155		
Background RH	360	1.34 (1.03,1.75)	0.032
Low RH	221	1.33 (0.96,1.84)	0.081
High RH	236	1.03 (0.76,1.40)	0.865
Low plus High RH	457	1.16 (0.92,1.48)	0.209

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**	
1987 Dioxin	**n**	**Number (%) Yes**	**Estimated Relative Risk (95% C.I.)[a]**	**p-Value**
Low	284	192 (67.6)	0.87 (0.79,0.96)	0.004
Medium	281	199 (70.8)		
High	287	170 (59.2)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 14-4. Analysis of Heart Disease (Excluding Essential Hypertension) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
817	0.92 (0.81,1.04)	0.159

[a] Relative risk for a twofold increase in 1987 dioxin.

The unadjusted Model 2 analysis revealed a significant inverse association between heart disease and initial dioxin (Table 14-4(c): Est. RR=0.79, p=0.001). The percentages of participants with heart disease in the low, medium, and high initial dioxin categories were 74.2, 61.5, and 55.0, respectively. After covariate adjustment, the results became nonsignificant (Table 14-4(d): p=0.249).

The Model 3 unadjusted analysis of heart disease revealed two significant contrasts: Ranch Hands in the background dioxin category versus Comparisons and Ranch Hands in the low dioxin category versus Comparisons (Table 14-4(e): Est. RR=1.43, p=0.005; Est. RR=1.48, p=0.011, respectively). The adjusted analysis showed a significant difference between Ranch Hands in the background dioxin category and Comparisons (Table 14-4(f): Adj. RR=1.34, p=0.032) and a marginally significant difference between Ranch Hands in the low dioxin category and Comparisons (Table 14-4(f): Adj. RR=1.33, p=0.081). The percentages of participants with heart disease for Ranch Hands in the background dioxin category, Ranch Hands in the low dioxin category, and Comparisons were 68.9, 70.0, and 61.1, respectively.

The Model 4 unadjusted analysis showed a significant inverse association between heart disease and 1987 dioxin (Table 14-4(g): Est. RR=0.87, p=0.004). The percentages of participants with heart disease in the low, medium, and high 1987 dioxin categories were 67.6, 70.8, and 59.2, respectively. The results became nonsignificant after adjusting for covariates (Table 14-4(h): p=0.159).

14.2.2.1.3 Myocardial Infarction

All unadjusted and adjusted Model 1 through Model 4 analyses of myocardial infarction were nonsignificant (Table 14-5(a–h): p>0.10 for each analysis).

Table 14-5. Analysis of Myocardial Infarction

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***74 (8.6)***	***1.04 (0.76,1.43)***	***0.786***
	Comparison	***1,232***	***102 (8.3)***		
Officer	Ranch Hand	334	28 (8.4)	0.96 (0.58,1.59)	0.882
	Comparison	484	42 (8.7)		
Enlisted Flyer	Ranch Hand	149	16 (10.7)	1.37 (0.65,2.87)	0.403
	Comparison	186	15 (8.1)		
Enlisted Groundcrew	Ranch Hand	376	30 (8.0)	1.00 (0.62,1.61)	0.987
	Comparison	562	45 (8.0)		

Table 14-5. Analysis of Myocardial Infarction (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1.02 (0.73,1.42)*	*0.915*
Officer	0.86 (0.50,1.46)	0.567
Enlisted Flyer	1.57 (0.72,3.43)	0.255
Enlisted Groundcrew	0.99 (0.59,1.67)	0.975

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	155	12 (7.7)	1.01 (0.79,1.28)	0.945
Medium	161	18 (11.2)		
High	160	13 (8.1)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
457	1.30 (0.95,1.77)	0.106

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race because of the sparse number of participants with a myocardial infarction.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,195	98 (8.2)		
Background RH	376	29 (7.7)	0.98 (0.63,1.51)	0.919
Low RH	233	19 (8.2)	0.99 (0.59,1.65)	0.958
High RH	243	24 (9.9)	1.18 (0.73,1.89)	0.496
Low plus High RH	476	43 (9.0)	1.08 (0.74,1.58)	0.689

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 14-5. Analysis of Myocardial Infarction (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,155		
Background RH	360	0.89 (0.55,1.43)	0.625
Low RH	221	0.84 (0.49,1.46)	0.544
High RH	236	1.39 (0.83,2.32)	0.215
Low plus High RH	457	1.09 (0.73,1.63)	0.673

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	284	21 (7.4)	1.03 (0.87,1.21)	0.740
Medium	281	23 (8.2)		
High	287	28 (9.8)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
817	1.16 (0.94,1.44)	0.170

[a] Relative risk for a twofold increase in 1987 dioxin.

14.2.2.1.4 Stroke or Transient Ischemic Attack

All analysis results of stroke or transient ischemic attack were nonsignificant (Table 14-6(a–h): p≥ 0.10 for each analysis).

Table 14-6. Analysis of Stroke or Transient Ischemic Attack

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	**Group**	**n**	**Number (%) Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***859***	***11 (1.3)***	***1.13 (0.51,2.50)***	***0.766***
	Comparison	***1,232***	***14 (1.1)***		
Officer	Ranch Hand	334	5 (1.5)	1.46 (0.42,5.07)	0.555
	Comparison	484	5 (1.0)		
Enlisted Flyer	Ranch Hand	149	0 (0.0)	--	0.330[a]
	Comparison	186	3 (1.6)		
Enlisted Groundcrew	Ranch Hand	376	6 (1.6)	1.50 (0.48,4.69)	0.483
	Comparison	562	6 (1.1)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a stroke or transient ischemic attack.
--: Results not presented because of the sparse number of participants with a stroke or transient ischemic attack.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	**Adjusted Relative Risk (95% C.I.)**	**p-Value**
All	***1.21 (0.51,2.85)***	***0.666***
Officer	1.18 (0.31,4.51)	0.806
Enlisted Flyer	--	--
Enlisted Groundcrew	1.80 (0.53,6.06)	0.345

--: Results not presented because of the sparse number of participants with a stroke or transient ischemic attack.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Number (%) Yes**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	155	1 (0.6)	1.22 (0.68,2.16)	0.513
Medium	161	2 (1.2)		
High	160	3 (1.9)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 14-6. Analysis of Stroke or Transient Ischemic Attack (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
457	1.33 (0.72,2.47)	0.379

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race and occupation because of the sparse number of Ranch Hands with a stroke or transient ischemic attack.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,195	14 (1.2)		
Background RH	376	5 (1.3)	1.13 (0.40,3.18)	0.816
Low RH	233	1 (0.4)	0.36 (0.05,2.78)	0.330
High RH	243	5 (2.1)	1.78 (0.63,5.02)	0.275
Low plus High RH	476	6 (1.3)	0.82 (0.25,2.68)	0.741

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,155		
Background RH	360	0.97 (0.30,3.16)	0.956
Low RH	221	0.42 (0.05,3.26)	0.404
High RH	236	2.65 (0.83,8.46)	0.100
Low plus High RH	457	1.08 (0.32,3.71)	0.900

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 14-6. Analysis of Stroke or Transient Ischemic Attack (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	284	4 (1.4)	0.99 (0.66,1.48)	0.957
Medium	281	2 (0.7)		
High	287	5 (1.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
817	1.15 (0.71,1.85)	0.578

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for occupation because of the sparse number of Ranch Hands with a stroke or transient ischemic attack.

14.2.2.2 Physical Examination Variables – Central Cardiac Function

14.2.2.2.1 Systolic Blood Pressure (Continuous)

All Model 1 and Model 2 analyses of systolic blood pressure in its continuous form showed no significant results (Table 14-7(a–d): p>0.23 for each analysis).

Table 14-7. Analysis of Systolic Blood Pressure (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***859***	***124.9***	***–0.7 --***	***0.383***
	Comparison	***1,232***	***125.6***		
Officer	Ranch Hand	334	125.9	–0.2 --	0.865
	Comparison	484	126.2		
Enlisted Flyer	Ranch Hand	149	127.0	–0.3 --	0.875
	Comparison	186	127.3		
Enlisted Groundcrew	Ranch Hand	376	123.1	–1.4 --	0.241
	Comparison	562	124.5		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 14-7. Analysis of Systolic Blood Pressure (Continuous) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***822***	***127.7***	***–0.6 --***	***0.415***
	Comparison	***1,189***	***128.4***		
Officer	Ranch Hand	322	127.2	–0.9 --	0.468
	Comparison	472	128.1		
Enlisted Flyer	Ranch Hand	140	128.7	0.1 --	0.967
	Comparison	178	128.6		
Enlisted Groundcrew	Ranch Hand	360	127.5	–0.7 --	0.574
	Comparison	539	128.2		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	155	125.8	126.4	0.049	–0.006 (0.005)	0.238
Medium	161	125.7	125.8			
High	160	124.2	123.6			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of systolic blood pressure versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	150	129.0	0.135	–0.000 (0.006)	0.983
Medium	150	130.2			
High	157	128.5			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of systolic blood pressure versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 14-7. Analysis of Systolic Blood Pressure (Continuous) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	**n**	**Mean[a]**	**Adj. Mean[ab]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]**	**p-Value[d]**
Comparison	1,195	125.6	125.5		
Background RH	376	124.4	125.4	–0.1 --	0.935
Low RH	233	126.2	125.9	0.4 --	0.730
High RH	243	124.4	123.4	–2.1 --	0.079
Low plus High RH	476	125.2	124.6	–0.9 --	0.346

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	**n**	**Adj. Mean[a]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]**	**p-Value[c]**
Comparison	1,155	128.5		
Background RH	360	128.5	0.0 --	0.990
Low RH	221	127.9	–0.6 --	0.651
High RH	236	127.0	–1.5 --	0.222
Low plus High RH	457	127.4	–1.1 --	0.262

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 14-7. Analysis of Systolic Blood Pressure (Continuous) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	284	124.0	<0.001	0.001 (0.003)	0.693
Medium	281	125.9			
High	287	124.8			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of systolic blood pressure versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	271	128.3	0.126	–0.005 (0.004)	0.165
Medium	271	127.2			
High	275	127.1			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of systolic blood pressure versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

The unadjusted Model 3 analysis showed a marginally significant difference between Ranch Hands in the high dioxin category and Comparisons (Table 14-7(e): difference of means=–2.1 mm Hg, p=0.079). Ranch Hands in the high dioxin category had a lower mean systolic blood pressure (123.4 mm Hg) than the Comparisons (125.5 mm Hg). The adjusted Model 3 analysis revealed no significant contrasts (Table 14-7(f): p>0.22 for each contrast).

Both the unadjusted and adjusted Model 4 analyses revealed no significant associations between 1987 dioxin and systolic blood pressure in its continuous form (Table 14-7(g,h): p>0.16 for each analysis).

14.2.2.2.2 Systolic Blood Pressure (Discrete)

The unadjusted and adjusted Model 1 analyses of systolic blood pressure in its discrete form showed no significant differences between Ranch Hands and Comparisons when examined across all occupations and within each occupation (Table 14-8(a,b): p>0.63 for each contrast).

Table 14-8. Analysis of Systolic Blood Pressure (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***181 (21.1)***	***0.99 (0.80,1.22)***	***0.914***
	Comparison	***1,232***	***262 (21.3)***		
Officer	Ranch Hand	334	78 (23.4)	1.01 (0.73,1.41)	0.944
	Comparison	484	112 (23.1)		
Enlisted Flyer	Ranch Hand	149	36 (24.2)	1.06 (0.64,1.76)	0.823
	Comparison	186	43 (23.1)		
Enlisted Groundcrew	Ranch Hand	376	67 (17.8)	0.92 (0.66,1.29)	0.638
	Comparison	562	107 (19.0)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.99 (0.79,1.24)***	***0.899***
Officer	0.95 (0.67,1.35)	0.784
Enlisted Flyer	1.13 (0.66,1.93)	0.661
Enlisted Groundcrew	0.96 (0.67,1.38)	0.832

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	155	40 (25.8)	0.83 (0.69,0.99)	0.031
Medium	161	36 (22.4)		
High	160	29 (18.1)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
457	0.89 (0.71,1.11)	0.296

[a] Relative risk for a twofold increase in initial dioxin.

Table 14-8. Analysis of Systolic Blood Pressure (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	**n**	**Number (%) High**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,195	253 (21.2)		
Background RH	376	74 (19.7)	1.00 (0.75,1.34)	0.998
Low RH	233	59 (25.3)	1.25 (0.90,1.73)	0.188
High RH	243	46 (18.9)	0.80 (0.56,1.14)	0.208
Low plus High RH	476	105 (22.1)	0.99 (0.76,1.29)	0.952

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Comparison	1,155		
Background RH	360	1.00 (0.73,1.37)	0.983
Low RH	221	1.12 (0.79,1.59)	0.532
High RH	236	0.84 (0.57,1.23)	0.365
Low plus High RH	457	0.96 (0.73,1.27)	0.791

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**	
1987 Dioxin	**n**	**Number (%) High**	**Estimated Relative Risk (95% C.I.)[a]**	**p-Value**
Low	284	54 (19.0)	1.00 (0.89,1.12)	0.956
Medium	281	66 (23.5)		
High	287	59 (20.6)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 14-8. Analysis of Systolic Blood Pressure (Discrete) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
817	0.88 (0.76,1.02)	0.099

[a] Relative risk for a twofold increase in 1987 dioxin.

A significant inverse association between discrete systolic blood pressure and initial dioxin was found in the unadjusted Model 2 analysis (Table 14-8(c): Est. RR=0.83, p=0.031). After adjusting for covariates, the results became nonsignificant (Table 14-8(d): p=0.296).

The unadjusted and adjusted Model 3 analyses of systolic blood pressure showed no significant contrasts between the Ranch Hand dioxin category and Comparisons (Table 14-8(e,f): p>0.18 for each contrast).

The unadjusted Model 4 results were nonsignificant (Table 14-8(g): p=0.956). After adjusting for covariates, the results became marginally significant (Table 14-8(h): Adj. RR=0.88, p=0.099). The percentages of participants with high discrete systolic blood pressures in the low, medium, and high 1987 dioxin categories were 19.0, 23.5, and 20.6, respectively.

14.2.2.2.3 Diastolic Blood Pressure (Continuous)

All Model 1 and Model 2 analyses of diastolic blood pressure in its continuous form showed no significant results (Table 14-9(a–d): p≥0.19 for each analysis).

The unadjusted Model 3 analysis of continuous diastolic blood pressure revealed a marginally significant difference between Ranch Hands in the high dioxin category and Comparisons (Table 14-9(e): difference of means=1.08 mm Hg, p=0.099). The adjusted results were nonsignificant (Table 14-9(f): p>0.13 for each contrast).

A significant positive association between 1987 dioxin and continuous diastolic blood pressure was found in the unadjusted Model 4 analysis (Table 14-9(g): slope=0.031, p=0.014). The mean diastolic blood pressure in the low, medium, and high 1987 dioxin categories was 73.97 mm Hg, 73.76 mm Hg, and 75.94 mm Hg, respectively. After adjusting for covariates, the results became nonsignificant (Table 14-9(h): p=0.315).

Table 14-9. Analysis of Diastolic Blood Pressure (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***859***	***74.55***	***–0.06 --***	***0.883***
	Comparison	***1,232***	***74.61***		
Officer	Ranch Hand	334	74.17	–0.04 --	0.952
	Comparison	484	74.21		
Enlisted Flyer	Ranch Hand	149	75.22	0.12 --	0.905
	Comparison	186	75.10		
Enlisted Groundcrew	Ranch Hand	376	74.63	–0.17 --	0.780
	Comparison	562	74.80		

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***822***	***75.68***	***0.06 --***	***0.889***
	Comparison	***1,189***	***75.62***		
Officer	Ranch Hand	322	75.29	–0.08 --	0.907
	Comparison	472	75.37		
Enlisted Flyer	Ranch Hand	140	76.47	0.33 --	0.752
	Comparison	178	76.13		
Enlisted Groundcrew	Ranch Hand	360	75.37	0.08 --	0.898
	Comparison	539	75.29		

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	155	74.07	74.24	0.023	0.025 (0.019)	0.190
Medium	161	75.16	75.17			
High	160	76.07	75.89			

[a] Transformed from square root scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on square root of diastolic blood pressure versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 14-9. Analysis of Diastolic Blood Pressure (Continuous) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	150	76.09	0.073	0.019 (0.023)	0.425
Medium	150	77.21			
High	157	77.40			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of diastolic blood pressure versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,195	74.58	74.57		
Background RH	376	73.87	74.14	–0.43 --	0.432
Low RH	233	74.26	74.19	–0.38 --	0.569
High RH	243	75.93	75.65	1.08 --	0.099
Low plus High RH	476	75.11	74.93	0.36 --	0.468

[a] Transformed from square root scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[d] P-value is based on difference of means on square root scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 14-9. Analysis of Diastolic Blood Pressure (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,155	75.67		
Background RH	360	75.56	–0.11 --	0.844
Low RH	221	75.23	–0.44 --	0.515
High RH	236	76.69	1.02 --	0.135
Low plus High RH	457	75.98	0.31 --	0.544

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	284	73.97	0.007	0.031 (0.013)	0.014
Medium	281	73.76			
High	287	75.94			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of diastolic blood pressure versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	271	75.59	0.061	0.016 (0.016)	0.315
Medium	271	75.01			
High	275	77.24			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of diastolic blood pressure versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

14.2.2.2.4 Diastolic Blood Pressure (Discrete)

All unadjusted and adjusted analyses of diastolic blood pressure in its dichotomous form were nonsignificant (Table 14-10(a–h): p>0.19 for each analysis).

Table 14-10. Analysis of Diastolic Blood Pressure (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***45 (5.2)***	***1.06 (0.71,1.58)***	***0.769***
	Comparison	***1,232***	***61 (5.0)***		
Officer	Ranch Hand	334	20 (6.0)	1.34 (0.72,2.49)	0.360
	Comparison	484	22 (4.5)		
Enlisted Flyer	Ranch Hand	149	8 (5.4)	1.26 (0.46,3.45)	0.649
	Comparison	186	8 (4.3)		
Enlisted Groundcrew	Ranch Hand	376	17 (4.5)	0.81 (0.44,1.49)	0.499
	Comparison	562	31 (5.5)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.02 (0.67,1.56)***	***0.916***
Officer	1.21 (0.62,2.35)	0.576
Enlisted Flyer	1.18 (0.41,3.37)	0.760
Enlisted Groundcrew	0.84 (0.44,1.59)	0.584

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	155	7 (4.5)	1.04 (0.79,1.37)	0.793
Medium	161	12 (7.5)		
High	160	10 (6.3)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

n	Analysis Results for Log_2 (Initial Dioxin) Adjusted Relative Risk (95% C.I.)[a]	p-Value
457	1.15 (0.80,1.67)	0.446

[a] Relative risk for a twofold increase in initial dioxin.

Table 14-10. Analysis of Diastolic Blood Pressure (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,195	59 (4.9)		
Background RH	376	15 (4.0)	0.85 (0.47,1.52)	0.576
Low RH	233	12 (5.2)	1.04 (0.55,1.96)	0.915
High RH	243	17 (7.0)	1.37 (0.78,2.41)	0.267
Low plus High RH	476	29 (6.1)	1.20 (0.75,1.90)	0.447

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,155		
Background RH	360	0.78 (0.41,1.48)	0.449
Low RH	221	0.91 (0.45,1.83)	0.792
High RH	236	1.46 (0.80,2.68)	0.221
Low plus High RH	457	1.16 (0.71,1.91)	0.551

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	284	14 (4.9)	1.14 (0.94,1.39)	0.198
Medium	281	9 (3.2)		
High	287	21 (7.3)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 14-10. Analysis of Diastolic Blood Pressure (Discrete) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
817	1.20 (0.89,1.61)	0.228

[a] Relative risk for a twofold increase in 1987 dioxin.

14.2.2.2.5 Heart Sounds

All Model 1 and Model 2 analyses of heart sounds were nonsignificant (Table 14-11(a–d): $p>0.11$ for each analysis).

Table 14-11. Analysis of Heart Sounds

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***31 (3.6)***	***0.71 (0.45,1.10)***	***0.116***
	Comparison	***1,232***	***62 (5.0)***		
Officer	Ranch Hand	334	11 (3.3)	0.60 (0.29,1.23)	0.164
	Comparison	484	26 (5.4)		
Enlisted Flyer	Ranch Hand	149	7 (4.7)	0.78 (0.30,2.08)	0.625
	Comparison	186	11 (5.9)		
Enlisted Groundcrew	Ranch Hand	376	13 (3.5)	0.77 (0.39,1.52)	0.452
	Comparison	562	25 (4.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.71 (0.45,1.13)***	***0.139***
Officer	0.60 (0.28,1.29)	0.190
Enlisted Flyer	0.65 (0.23,1.84)	0.419
Enlisted Groundcrew	0.86 (0.42,1.74)	0.675

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	155	6 (3.9)	1.01 (0.73,1.40)	0.958
Medium	161	10 (6.2)		
High	160	6 (3.8)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 14-11. Analysis of Heart Sounds (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
457	1.28 (0.83,1.98)	0.266

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,195	60 (5.0)		
Background RH	376	9 (2.4)	0.48 (0.24,0.99)	0.047
Low RH	233	10 (4.3)	0.84 (0.42,1.67)	0.622
High RH	243	12 (4.9)	0.94 (0.50,1.79)	0.857
Low plus High RH	476	22 (4.6)	0.89 (0.54,1.48)	0.656

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,155		
Background RH	360	0.45 (0.21,0.97)	0.041
Low RH	221	0.80 (0.39,1.61)	0.528
High RH	236	1.05 (0.52,2.11)	0.901
Low plus High RH	457	0.92 (0.54,1.56)	0.750

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 14-11. Analysis of Heart Sounds (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	284	8 (2.8)	1.16 (0.92,1.46)	0.220
Medium	281	9 (3.2)		
High	287	14 (4.9)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
Analysis Results for Log_2 (1987 Dioxin + 1)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
817	1.24 (0.89,1.73)	0.193

[a] Relative risk for a twofold increase in 1987 dioxin.

The unadjusted and adjusted Model 3 analyses each showed a significant difference between Ranch Hands in the background dioxin category and Comparisons (Table 14-11(e,f): Est. RR=0.48, p=0.047; Adj. RR=0.45, p=0.041, respectively). The percentage of participants with abnormal heart sounds was lower for Ranch Hands in the background dioxin category (2.4%) than for Comparisons (5.0%).

Model 4 unadjusted and adjusted analyses showed no significant association between heart sounds and 1987 dioxin (Table 14-11(g,h): p>0.19 for each analysis).

14.2.2.2.6 Overall Electrocardiograph

The unadjusted and adjusted Model 1 analyses of overall ECG showed no overall group difference between Ranch Hands and Comparisons (Table 14-12(a,b): p>0.68 for each contrast). Stratifying by occupation revealed a marginally significant group difference within the enlisted groundcrew stratum for both the unadjusted and adjusted analyses (Table 14-12(a,b): Est. RR=0.77, p=0.096; Adj. RR=0.76, p=0.095, respectively). The percentage of enlisted groundcrew with abnormal overall ECG results was lower for Ranch Hands (23.4%) than for Comparisons (28.3%).

Both the unadjusted and adjusted Model 2 analyses of overall ECG were nonsignificant (Table 14-12(c,d): p>0.17 for each analysis).

The unadjusted Model 3 analyses of overall ECG did not show any of the Ranch Hand categories to be significantly different from the Comparison group (Table 14-12(e): p>0.60 for each contrast). After adjusting for covariates, a marginally significant difference between Ranch Hands in the low dioxin category and Comparisons was revealed (Table 14-12(f): Adj. RR=0.73, p=0.063). The percentage of abnormal overall ECG results was lower for Ranch Hands (30.9%) than for Comparisons (31.2%). Both the unadjusted and adjusted Model 4 analyses were nonsignificant (Table 14-12(g,h): p>0.39 for each analysis).

Table 14-12. Analysis of Overall Electrocardiograph (ECG)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*859*	*268 (31.2)*	*1.00 (0.83,1.21)*	*0.988*
	Comparison	*1,232*	*384 (31.2)*		
Officer	Ranch Hand	334	120 (35.9)	1.10 (0.82,1.48)	0.506
	Comparison	484	163 (33.7)		
Enlisted Flyer	Ranch Hand	149	60 (40.3)	1.35 (0.86,2.11)	0.190
	Comparison	186	62 (33.3)		
Enlisted Groundcrew	Ranch Hand	376	88 (23.4)	0.77 (0.57,1.05)	0.096
	Comparison	562	159 (28.3)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	*0.96 (0.78,1.18)*	*0.688*
Officer	1.07 (0.79,1.47)	0.655
Enlisted Flyer	1.24 (0.76,2.00)	0.389
Enlisted Groundcrew	0.76 (0.55,1.05)	0.095

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	155	51 (32.9)	0.90 (0.77,1.05)	0.171
Medium	161	47 (29.2)		
High	160	48 (30.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
457	1.14 (0.93,1.39)	0.200

[a] Relative risk for a twofold increase in initial dioxin.

Table 14-12. Analysis of Overall Electrocardiograph (ECG) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,195	373 (31.2)		
Background RH	376	118 (31.4)	1.06 (0.82,1.36)	0.659
Low RH	233	72 (30.9)	0.98 (0.72,1.33)	0.883
High RH	243	74 (30.5)	0.92 (0.68,1.25)	0.602
Low plus High RH	476	146 (30.7)	0.95 (0.75,1.20)	0.659

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,155		
Background RH	360	1.00 (0.76,1.32)	0.980
Low RH	221	0.73 (0.52,1.02)	0.063
High RH	236	1.10 (0.78,1.54)	0.578
Low plus High RH	457	0.90 (0.70,1.16)	0.423

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	284	84 (29.6)	0.96 (0.87,1.06)	0.391
Medium	281	93 (33.1)		
High	287	87 (30.3)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 14-12. Analysis of Overall Electrocardiograph (ECG) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
817	1.02 (0.89,1.17)	0.753

[a] Relative risk for a twofold increase in 1987 dioxin.

14.2.2.2.7 Right Bundle Branch Block

All unadjusted and adjusted analysis results of right bundle branch block were nonsignificant (Table 14-13(a–h): p>0.27 for each analysis).

Table 14-13. Analysis of Right Bundle Branch Block

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***21 (2.4)***	***0.91 (0.52,1.58)***	***0.739***
	Comparison	***1,232***	***33 (2.7)***		
Officer	Ranch Hand	334	8 (2.4)	0.89 (0.36,2.17)	0.796
	Comparison	484	13 (2.7)		
Enlisted Flyer	Ranch Hand	149	8 (5.4)	1.45 (0.51,4.10)	0.482
	Comparison	186	7 (3.8)		
Enlisted Groundcrew	Ranch Hand	376	5 (1.3)	0.57 (0.20,1.61)	0.288
	Comparison	562	13 (2.3)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.88 (0.49,1.56)***	***0.650***
Officer	0.89 (0.36,2.22)	0.807
Enlisted Flyer	1.47 (0.49,4.44)	0.493
Enlisted Groundcrew	0.55 (0.19,1.59)	0.271

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	155	5 (3.2)	0.93 (0.59,1.46)	0.747
Medium	161	4 (2.5)		
High	160	3 (1.9)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 14-13. Analysis of Right Bundle Branch Block (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
462	1.12 (0.62,2.04)	0.707

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race and family history of heart disease before age 45 because of the sparse number of Ranch Hands with a right bundle branch block.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,195	31 (2.6)		
Background RH	376	9 (2.4)	0.93 (0.44,1.98)	0.852
Low RH	233	5 (2.1)	0.82 (0.32,2.14)	0.688
High RH	243	7 (2.9)	1.10 (0.48,2.54)	0.818
Low plus High RH	476	12 (2.5)	0.96 (0.48,1.89)	0.895

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,155		
Background RH	360	1.04 (0.47,2.29)	0.920
Low RH	221	0.55 (0.19,1.60)	0.273
High RH	236	1.19 (0.49,2.88)	0.704
Low plus High RH	457	0.82 (0.39,1.71)	0.594

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 14-13. Analysis of Right Bundle Branch Block (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	284	6 (2.1)	1.03 (0.77,1.38)	0.845
Medium	281	8 (2.8)		
High	287	7 (2.4)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
817	1.02 (0.69,1.50)	0.922

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race because of the sparse number of Ranch Hands with a right bundle branch block.

14.2.2.2.8 Left Bundle Branch Block

The unadjusted and adjusted Model 1 analyses of left bundle branch block were nonsignificant (Table 14-14(a,b): p≥0.15 for each contrast).

Table 14-14. Analysis of Left Bundle Branch Block

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***5 (0.6)***	***0.60 (0.21,1.70)***	***0.317***
	Comparison	***1,232***	***12 (1.0)***		
Officer	Ranch Hand	334	2 (0.6)	0.48 (0.10,2.39)	0.370
	Comparison	484	6 (1.2)		
Enlisted Flyer	Ranch Hand	149	1 (0.7)	--	0.911[a]
	Comparison	186	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	376	2 (0.5)	0.50 (0.10,2.47)	0.391
	Comparison	562	6 (1.1)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a left bundle branch block.
--: Results not presented because of the sparse number of participants with a left bundle branch block.

Table 14-14. Analysis of Left Bundle Branch Block (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.47 (0.15,1.50)***	***0.182***
Officer	0.21 (0.02,1.76)	0.150
Enlisted Flyer	--	--
Enlisted Groundcrew	0.56 (0.11,2.83)	0.479

--: Results not presented because of the sparse number of participants with a left bundle branch block.

Note: Results are not adjusted for race because of the sparse number of participants with a left bundle branch block.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	155	1 (0.6)	0.21 (0.01,6.22)	0.213
Medium	161	0 (0.0)		
High	160	0 (0.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)	p-Value
--	--	--

--: Results not presented because of the sparse number of Ranch Hands with a left bundle branch block.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,195	12 (1.0)		
Background RH	376	4 (1.1)	1.17 (0.37,3.68)	0.792
Low RH	233	1 (0.4)	0.42 (0.05,3.23)	0.403
High RH	243	0 (0.0)	--	0.237[c]
Low plus High RH	476	1 (0.2)	--	0.174[c]

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with left bundle branch block.
--: Results not presented because of the sparse number of participants with a left bundle branch block.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 14-14. Analysis of Left Bundle Branch Block (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,155		
Background RH	360	0.87 (0.23,3.33)	0.838
Low RH	221	0.37 (0.05,2.91)	0.341
High RH	236	--	--
Low plus High RH	457	--	--

[a] Relative risk and confidence interval relative to Comparisons.
--: Results not presented because of the sparse number of participants with a left bundle branch block.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for race because of the sparse number of participants with a left bundle branch block.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	284	1 (0.4)	0.69 (0.35,1.36)	0.271
Medium	281	4 (1.4)		
High	287	0 (0.0)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
823	0.56 (0.23,1.39)	0.199

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race and diabetic class because of the sparse number of participants with a left bundle branch block.

The unadjusted Model 2 analysis showed no significant association between left bundle branch block and initial dioxin (Table 14-14(c): p=0.213). Because of a sparse number of Ranch Hands with a left bundle branch block, the adjusted Model 2 analysis was not performed.

All unadjusted and adjusted Model 3 and 4 analyses were nonsignificant (Table 14-14(e–h): p>0.17 for each analysis).

14.2.2.2.9 Non-Specific ST- and T-Wave Changes

All unadjusted and adjusted analyses of non-specific ST- and T-wave changes were nonsignificant (Table 14-15(a–h): p≥0.18 for each analysis).

Table 14-15. Analysis of Non-Specific ST- and T-Wave Changes

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***160 (18.6)***	***1.04 (0.83,1.30)***	***0.724***
	Comparison	***1,232***	***222 (18.0)***		
Officer	Ranch Hand	334	70 (21.0)	1.09 (0.77,1.53)	0.641
	Comparison	484	95 (19.6)		
Enlisted Flyer	Ranch Hand	149	33 (22.1)	1.27 (0.74,2.17)	0.380
	Comparison	186	34 (18.3)		
Enlisted Groundcrew	Ranch Hand	376	57 (15.2)	0.90 (0.63,1.29)	0.570
	Comparison	562	93 (16.5)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.00 (0.79,1.27)***	***0.984***
Officer	1.03 (0.71,1.48)	0.882
Enlisted Flyer	1.22 (0.69,2.14)	0.495
Enlisted Groundcrew	0.88 (0.60,1.29)	0.517

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	155	32 (20.6)	0.91 (0.76,1.08)	0.280
Medium	161	34 (21.1)		
High	160	31 (19.4)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
457	1.15 (0.91,1.44)	0.237

[a] Relative risk for a twofold increase in initial dioxin.

Table 14-15. Analysis of Non-Specific ST- and T-Wave Changes (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,195	218 (18.2)		
Background RH	376	59 (15.7)	0.91 (0.66,1.25)	0.545
Low RH	233	47 (20.2)	1.12 (0.78,1.59)	0.537
High RH	243	50 (20.6)	1.08 (0.76,1.52)	0.677
Low plus High RH	476	97 (20.4)	1.10 (0.84,1.44)	0.502

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,155		
Background RH	360	0.82 (0.58,1.15)	0.242
Low RH	221	0.91 (0.62,1.32)	0.614
High RH	236	1.26 (0.86,1.84)	0.238
Low plus High RH	457	1.07 (0.80,1.43)	0.628

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	284	43 (15.1)	1.06 (0.94,1.19)	0.361
Medium	281	52 (18.5)		
High	287	61 (21.3)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 14-15. Analysis of Non-Specific ST- and T-Wave Changes (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
817	1.12 (0.95,1.32)	0.180

[a] Relative risk for a twofold increase in 1987 dioxin.

14.2.2.2.10 Bradycardia

The Model 1 and 2 analyses of bradycardia did not show a significant association with dioxin in either the unadjusted or adjusted analysis (Table 14-16(a–d): p≥0.12 for each analysis).

Table 14-16. Analysis of Bradycardia

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***24 (2.8)***	***0.69 (0.42,1.14)***	***0.142***
	Comparison	***1,232***	***49 (4.0)***		
Officer	Ranch Hand	334	15 (4.5)	0.69 (0.36,1.29)	0.245
	Comparison	484	31 (6.4)		
Enlisted Flyer	Ranch Hand	149	5 (3.4)	1.26 (0.36,4.43)	0.722
	Comparison	186	5 (2.7)		
Enlisted Groundcrew	Ranch Hand	376	4 (1.1)	0.45 (0.15,1.40)	0.170
	Comparison	562	13 (2.3)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.69 (0.41,1.16)***	***0.151***
Officer	0.74 (0.38,1.42)	0.360
Enlisted Flyer	1.14 (0.32,4.09)	0.846
Enlisted Groundcrew	0.36 (0.10,1.30)	0.120

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	155	4 (2.6)	0.86 (0.44,1.65)	0.631
Medium	161	2 (1.2)		
High	160	1 (0.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 14-16. Analysis of Bradycardia (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
466	0.98 (0.44,2.22)	0.971

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race, diabetic class, and family history of heart disease before age 45 because of the sparse number of Ranch Hands with bradycardia.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,195	47 (3.9)		
Background RH	376	16 (4.3)	0.95 (0.53,1.71)	0.867
Low RH	233	5 (2.1)	0.55 (0.21,1.39)	0.204
High RH	243	2 (0.8)	0.23 (0.05,0.95)	0.042
Low plus High RH	476	7 (1.5)	0.35 (0.14,0.85)	0.020

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,155		
Background RH	360	0.81 (0.44,1.49)	0.497
Low RH	221	0.49 (0.17,1.40)	0.183
High RH	236	0.35 (0.08,1.50)	0.156
Low plus High RH	457	0.41 (0.16,1.05)	0.062

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 14-16. Analysis of Bradycardia (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	284	11 (3.9)	0.77 (0.56,1.05)	0.084
Medium	281	9 (3.2)		
High	287	3 (1.0)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
828	0.98 (0.65,1.49)	0.932

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for family history of heart disease before age 45 because of the sparse number of Ranch Hands with bradycardia.

The unadjusted Model 3 analysis of bradycardia revealed two significant contrasts: Ranch Hands in the high dioxin category versus Comparisons and Ranch Hands in the low plus high dioxin category versus Comparisons (Table 14-16(e): Est. RR=0.23, p=0.042; Est. RR=0.35, p=0.020, respectively). The percentage of participants with bradycardia was higher for Comparisons (3.9%) than for Ranch Hands in the high dioxin category (0.8%) or Ranch Hands in the low plus high dioxin category (1.5%). After covariate adjustment, there was a marginally significant difference between Ranch Hands in the low plus high dioxin category and Comparisons (Table 14-16(f): Adj. RR=0.41, p=0.062).

The unadjusted Model 4 analysis of bradycardia revealed a marginally significant inverse association between bradycardia and 1987 dioxin (Table 14-16(g): Est. RR=0.77, p=0.084). The percentages of participants with bradycardia in the low, medium, and high 1987 dioxin categories were 3.9, 3.2, and 1.0, respectively. After covariate adjustment, the results became nonsignificant (Table 14-16(h): p=0.932).

14.2.2.2.11 Tachycardia

The unadjusted and adjusted Model 1 analyses of tachycardia were nonsignificant (Table 14-17(a,b): p>0.12 for each contrast).

Table 14-17. Analysis of Tachycardia

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***6 (0.7)***	***2.16 (0.61,7.68)***	***0.228***
	Comparison	***1,232***	***4 (0.3)***		
Officer	Ranch Hand	334	1 (0.3)	1.45 (0.09,23.27)	0.793
	Comparison	484	1 (0.2)		
Enlisted Flyer	Ranch Hand	149	3 (2.0)	--	0.174[a]
	Comparison	186	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	376	2 (0.5)	1.00 (0.17,5.99)	0.997
	Comparison	562	3 (0.5)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with tachycardia.
--: Results not presented because of the sparse number of participants with tachycardia.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***2.94 (0.69,12.51)***	***0.129***
Officer	--	--
Enlisted Flyer	--	--
Enlisted Groundcrew	1.54 (0.19,12.63)	0.685

--: Results not presented because of the sparse number of participants with tachycardia.

Note: Results are not adjusted for family history of heart disease because of the sparse number of participants with tachycardia.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	155	0 (0.0)	1.38 (0.72,2.68)	0.340
Medium	161	1 (0.6)		
High	160	3 (1.9)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 14-17. Analysis of Tachycardia (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)	p-Value
--	--	--

--: Results not presented because of the sparse number of Ranch Hands with tachycardia.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,195	3 (0.3)		
Background RH	376	1 (0.3)	1.33 (0.14,13.00)	0.806
Low RH	233	0 (0.0)	--	0.999[c]
High RH	243	4 (1.6)	5.30 (1.15,24.53)	0.033
Low plus High RH	476	4 (0.8)	--	0.206[c]

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with tachycardia.
--: Results not presented because of the sparse number of participants with tachycardia.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,155		
Background RH	360	2.01 (0.16,24.61)	0.585
Low RH	221	--	--
High RH	236	8.10 (1.19,55.01)	0.032
Low plus High RH	457	--	--

[a] Relative risk and confidence interval relative to Comparisons.
--: Results not presented because of the sparse number of participants with tachycardia.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for family history of heart disease because of the sparse number of participants with tachycardia.

Table 14-17. Analysis of Tachycardia (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	284	1 (0.4)	1.56 (0.92,2.63)	0.111
Medium	281	0 (0.0)		
High	287	4 (1.4)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
Analysis Results for Log_2 (1987 Dioxin + 1)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
825	1.55 (0.85,2.84)	0.165

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for occupation, current alcohol use, personality type, family history of heart disease, and diabetic class because of the sparse number of participants with tachycardia.

The unadjusted Model 2 analysis showed no significant association between tachycardia and initial dioxin (Table 14-17(c): p=0.340). Because of a sparse number of Ranch Hands with tachycardia, the adjusted Model 2 analysis was not performed.

The unadjusted and adjusted Model 3 analyses each showed a significant difference between Ranch Hands in the high dioxin category and Comparisons (Table 14-17(e,f): Est. RR=5.30, p=0.033; Adj. RR=8.10, p=0.032, respectively). The percentage of participants with tachycardia for Ranch Hands in the high dioxin categories was 1.6 versus 0.3 percent for Comparisons.

The unadjusted and adjusted Model 4 analyses were nonsignificant (Table 14-17(g,h): p>0.11 for each analysis).

14.2.2.2.12 Arrhythmia

All unadjusted and adjusted analyses of arrhythmia were nonsignificant (Table 14-18(a–h): p>0.11 for each analysis).

Table 14-18. Analysis of Arrhythmia

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***51 (5.9)***	***1.08 (0.74,1.57)***	***0.686***
	Comparison	***1,232***	***68 (5.5)***		
Officer	Ranch Hand	334	25 (7.5)	1.49 (0.84,2.63)	0.176
	Comparison	484	25 (5.2)		
Enlisted Flyer	Ranch Hand	149	13 (8.7)	1.39 (0.61,3.13)	0.433
	Comparison	186	12 (6.5)		
Enlisted Groundcrew	Ranch Hand	376	13 (3.5)	0.61 (0.32,1.19)	0.147
	Comparison	562	31 (5.5)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.02 (0.69,1.52)***	***0.913***
Officer	1.39 (0.75,2.55)	0.296
Enlisted Flyer	1.26 (0.54,2.97)	0.591
Enlisted Groundcrew	0.62 (0.31,1.25)	0.180

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log₂ (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	155	13 (8.4)	0.81 (0.60,1.10)	0.158
Medium	161	11 (6.8)		
High	160	8 (5.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
457	1.00 (0.68,1.48)	0.981

[a] Relative risk for a twofold increase in initial dioxin.

Table 14-18. Analysis of Arrhythmia (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,195	65 (5.4)		
Background RH	376	18 (4.8)	0.90 (0.53,1.54)	0.703
Low RH	233	19 (8.2)	1.54 (0.90,2.61)	0.114
High RH	243	13 (5.3)	0.96 (0.52,1.77)	0.886
Low plus High RH	476	32 (6.7)	1.21 (0.77,1.88)	0.409

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,155		
Background RH	360	0.87 (0.49,1.57)	0.647
Low RH	221	1.17 (0.65,2.11)	0.596
High RH	236	1.10 (0.57,2.12)	0.774
Low plus High RH	457	1.13 (0.70,1.83)	0.604

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	284	14 (4.9)	0.99 (0.82,1.20)	0.932
Medium	281	20 (7.1)		
High	287	16 (5.6)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 14-18. Analysis of Arrhythmia (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
817	1.12 (0.85,1.49)	0.422

[a] Relative risk for a twofold increase in 1987 dioxin.

14.2.2.2.13 Evidence of Prior Myocardial Infarction

The Model 1 unadjusted and adjusted analyses of prior myocardial infarction from the ECG showed no significant group differences over all participants or within each occupational stratum (Table 14-19(a,b): p>0.64 for each contrast).

Table 14-19. Analysis of Evidence of Prior Myocardial Infarction

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***34 (4.0)***	***0.92 (0.59,1.42)***	***0.698***
	Comparison	***1,232***	***53 (4.3)***		
Officer	Ranch Hand	334	15 (4.5)	0.94 (0.48,1.83)	0.862
	Comparison	484	23 (4.8)		
Enlisted Flyer	Ranch Hand	149	7 (4.7)	0.97 (0.35,2.67)	0.952
	Comparison	186	9 (4.8)		
Enlisted Groundcrew	Ranch Hand	376	12 (3.2)	0.85 (0.41,1.75)	0.657
	Comparison	562	21 (3.7)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.90 (0.56,1.43)***	***0.649***
Officer	0.88 (0.43,1.78)	0.718
Enlisted Flyer	1.02 (0.35,2.96)	0.972
Enlisted Groundcrew	0.86 (0.40,1.85)	0.709

Table 14-19. Analysis of Evidence of Prior Myocardial Infarction (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	155	5 (3.2)	1.05 (0.75,1.46)	0.793
Medium	161	9 (5.6)		
High	160	7 (4.4)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
457	1.84 (1.13,2.99)	0.012

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race because of the sparse number of Ranch Hands with evidence of a prior myocardial infarction.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,195	53 (4.4)		
Background RH	376	12 (3.2)	0.75 (0.39,1.42)	0.374
Low RH	233	11 (4.7)	1.06 (0.54,2.06)	0.867
High RH	243	10 (4.1)	0.88 (0.44,1.76)	0.722
Low plus High RH	476	21 (4.4)	0.96 (0.57,1.62)	0.891

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 14-19. Analysis of Evidence of Prior Myocardial Infarction (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Comparison	1,155		
Background RH	360	0.69 (0.34,1.37)	0.285
Low RH	221	0.79 (0.39,1.61)	0.524
High RH	236	1.11 (0.52,2.36)	0.783
Low plus High RH	457	0.94 (0.54,1.65)	0.841

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**	
1987 Dioxin	**n**	**Number (%) Yes**	**Estimated Relative Risk (95% C.I.)[a]**	**p-Value**
Low	284	7 (2.5)	1.09 (0.87,1.38)	0.447
Medium	281	12 (4.3)		
High	287	14 (4.9)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
817	1.33 (0.95,1.87)	0.089

[a] Relative risk for a twofold increase in 1987 dioxin.

The unadjusted Model 2 analysis revealed no significant association between initial dioxin and prior myocardial infarction (Table 14-19(c): p=0.793). After adjusting for covariates, the results became significant (Table 14-19(d): Adj. RR=1.84, p=0.012). The percentages of participants with evidence of prior myocardial infarction in the low, medium, and high initial dioxin categories were 3.2, 5.6, and 4.4, respectively.

The unadjusted and adjusted Model 3 analyses of prior myocardial infarction did not show any of the Ranch Hand categories to be significantly different from the Comparisons (Table 14-19(e,f): p>0.28 for each contrast).

The unadjusted Model 4 analysis revealed no significant association between 1987 dioxin and evidence of prior myocardial infarction (Table 14-19(g): p=0.447). After adjusting for covariates, the results became marginally significant (Table 14-19(h): Adj. RR=1.33, p=0.089). The percentages of participants with evidence of prior myocardial infarction in the low, medium, and high 1987 dioxin categories were 2.5, 4.3, and 4.9, respectively.

14.2.2.2.14 ECG: Other Diagnoses

The Model 1 unadjusted and adjusted analyses of other ECG diagnoses showed no significant group differences over all participants or within each occupational stratum (Table 14-20(a,b): p>0.15 for each contrast).

Table 14-20. Analysis of ECG: Other Diagnoses

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***3 (0.3)***	***4.31 (0.45,41.55)***	***0.168***
	Comparison	***1,232***	***1 (0.1)***		
Officer	Ranch Hand	334	1 (0.3)	--	0.852[a]
	Comparison	484	0 (0.0)		
Enlisted Flyer	Ranch Hand	149	0 (0.0)	--	--
	Comparison	186	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	376	2 (0.5)	3.00 (0.27,33.20)	0.370
	Comparison	562	1 (0.2)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with other abnormal ECG diagnoses.

--: Results not presented because of the sparse number of participants with other abnormal ECG diagnoses.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***4.67 (0.47,46.79)***	***0.153***
Officer	--	--
Enlisted Flyer	--	--
Enlisted Groundcrew	3.29 (0.28,38.94)	0.346

--: Results not presented because of the sparse number of participants with other abnormal ECG diagnoses.

Note: Results are not adjusted for family history of heart disease before age 45 and diabetic class because of the sparse number of participants with other abnormal ECG diagnoses. Results for all occupations combined also are not adjusted for occupation because of the sparse number of participants with other abnormal ECG diagnoses.

Table 14-20. Analysis of ECG: Other Diagnoses (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	155	0 (0.0)	1.53 (0.62,3.79)	0.381
Medium	161	0 (0.0)		
High	160	2 (1.3)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)	p-Value
--	--	--

--: Results not presented because of the sparse number of Ranch Hands with other abnormal ECG diagnoses.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,195	1 (0.1)		
Background RH	376	1 (0.3)	2.59 (0.16,41.85)	0.503
Low RH	233	0 (0.0)	--	0.999[c]
High RH	243	2 (0.8)	12.49 (1.10,142.56)	0.042
Low plus High RH	476	2 (0.4)	--	0.409[c]

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with other abnormal ECG diagnoses.
--: Results not presented because of the sparse number of participants with other abnormal ECG diagnoses.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 14-20. Analysis of ECG: Other Diagnoses (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Comparison	1,186		
Background RH	368	2.89 (0.16,52.97)	0.474
Low RH	227	--	--
High RH	239	12.41 (1.00,154.15)	0.050
Low plus High RH	466	--	--

[a] Relative risk and confidence interval relative to Comparisons.
--: Results not presented because of the sparse number of participants with other abnormal ECG diagnoses.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for occupation, family history of heart disease before age 45, and diabetic class because of the sparse number of participants with other abnormal ECG diagnoses.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**	
1987 Dioxin	**n**	**Number (%) Yes**	**Estimated Relative Risk (95% C.I.)[a]**	**p-Value**
Low	284	1 (0.4)	1.27 (0.63,2.59)	0.512
Medium	281	0 (0.0)		
High	287	2 (0.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
834	1.47 (0.58,3.73)	0.413

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for occupation, current cigarette smoking, family history of heart disease before age 45, and diabetic class because of the sparse number of Ranch Hands with other abnormal ECG diagnoses.

The unadjusted Model 2 analysis revealed no significant results (Table 14-20(c): p=0.381). Because of the sparse number of Ranch Hands with other ECG diagnoses, the adjusted Model 2 analysis was not performed.

The unadjusted and adjusted Model 3 analyses each revealed a significant difference between Ranch Hands in the high dioxin category and Comparisons (Table 14-20(e,f): Est. RR=12.49, p=0.042; Adj. RR=12.41, p=0.050, respectively). The percentage of Ranch Hands in the high dioxin category was 0.8 versus 0.1 percent for the Comparisons.

Both the unadjusted and adjusted Model 4 analyses did not reveal a significant association between 1987 dioxin and other ECG diagnoses (Table 14-20(g,h): p<0.41 for each analysis).

14.2.2.3 Physical Examination Variables – Peripheral Vascular Function

14.2.2.3.1 Funduscopic Examination

The unadjusted and adjusted Model 1 analyses of funduscopic examination did not reveal a group difference between Ranch Hands and Comparisons when all occupations were combined (Table 14-21(a,b): p>0.56 for each contrast). Stratifying by occupation revealed a significant group difference within the enlisted groundcrew stratum in both the unadjusted and adjusted analyses (Table 14-21(a,b): Est. RR=0.62, p=0.033; Adj. RR=0.62, p=0.047, respectively). Ranch Hand enlisted groundcrew had fewer abnormal funduscopic examination results (8.8%) than did Comparison enlisted groundcrew (13.3%).

Table 14-21. Analysis of Funduscopic Examination

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***858***	***105 (12.2)***	***0.96 (0.74,1.25)***	***0.767***
	Comparison	***1,231***	***156 (12.7)***		
Officer	Ranch Hand	333	42 (12.6)	1.28 (0.83,1.99)	0.267
	Comparison	484	49 (10.1)		
Enlisted Flyer	Ranch Hand	149	30 (20.1)	1.21 (0.69,2.09)	0.508
	Comparison	185	32 (17.3)		
Enlisted Groundcrew	Ranch Hand	376	33 (8.8)	0.62 (0.41,0.96)	0.033
	Comparison	562	75 (13.3)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.92 (0.69,1.22)***	***0.562***
Officer	1.27 (0.79,2.02)	0.321
Enlisted Flyer	1.06 (0.59,1.91)	0.852
Enlisted Groundcrew	0.62 (0.39,0.99)	0.047

Table 14-21. Analysis of Funduscopic Examination (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	155	20 (12.9)	0.93 (0.76,1.15)	0.520
Medium	161	24 (14.9)		
High	160	18 (11.3)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
457	1.14 (0.87,1.50)	0.342

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,194	149 (12.5)		
Background RH	375	43 (11.5)	0.99 (0.69,1.43)	0.963
Low RH	233	30 (12.9)	1.02 (0.67,1.56)	0.921
High RH	243	32 (13.2)	0.98 (0.65,1.49)	0.933
Low plus High RH	476	62 (13.0)	1.00 (0.73,1.38)	0.993

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 14-21. Analysis of Funduscopic Examination (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Comparison	1,154		
Background RH	359	1.04 (0.70,1.55)	0.842
Low RH	221	0.82 (0.52,1.30)	0.402
High RH	236	0.95 (0.60,1.51)	0.836
Low plus High RH	457	0.89 (0.63,1.26)	0.500

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**	
1987 Dioxin	**n**	**Number (%) Abnormal**	**Estimated Relative Risk (95% C.I.)[a]**	**p-Value**
Low	283	30 (10.6)	1.00 (0.87,1.15)	0.951
Medium	281	36 (12.8)		
High	287	39 (13.6)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
816	1.03 (0.85,1.24)	0.767

[a] Relative risk for a twofold increase in 1987 dioxin.

The unadjusted and adjusted analyses in Models 2 through 4 were nonsignificant (Table 14-21(c–h): p>0.34 for each analysis).

14.2.2.3.2 Carotid Bruits

All Model 1 through 4 unadjusted and adjusted analyses were nonsignificant (Table 14-22(a–h): p>0.21 for each analysis).

Table 14-22. Analysis of Carotid Bruits

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***23 (2.7)***	***1.00 (0.58,1.71)***	***0.999***
	Comparison	***1,232***	***33 (2.7)***		
Officer	Ranch Hand	334	6 (1.8)	0.72 (0.27,1.94)	0.515
	Comparison	484	12 (2.5)		
Enlisted Flyer	Ranch Hand	149	8 (5.4)	2.05 (0.66,6.41)	0.215
	Comparison	186	5 (2.7)		
Enlisted Groundcrew	Ranch Hand	376	9 (2.4)	0.84 (0.37,1.91)	0.673
	Comparison	562	16 (2.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.94 (0.53,1.65)***	***0.823***
Officer	0.72 (0.26,1.99)	0.524
Enlisted Flyer	1.94 (0.58,6.46)	0.283
Enlisted Groundcrew	0.78 (0.33,1.86)	0.578

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	155	3 (1.9)	1.06 (0.70,1.59)	0.797
Medium	161	5 (3.1)		
High	160	5 (3.1)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
457	1.15 (0.62,2.11)	0.658

[a] Relative risk for a twofold increase in initial dioxin.

Table 14-22. Analysis of Carotid Bruits (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,195	31 (2.6)		
Background RH	376	9 (2.4)	0.93 (0.44,1.98)	0.853
Low RH	233	5 (2.1)	0.82 (0.32,2.14)	0.687
High RH	243	8 (3.3)	1.27 (0.57,2.80)	0.561
Low plus High RH	476	13 (2.7)	1.02 (0.53,2.00)	0.943

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,155		
Background RH	360	1.06 (0.47,2.38)	0.893
Low RH	221	0.69 (0.25,1.86)	0.460
High RH	236	1.01 (0.41,2.45)	0.991
Low plus High RH	457	0.84 (0.41,1.71)	0.625

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	284	7 (2.5)	1.02 (0.77,1.36)	0.897
Medium	281	7 (2.5)		
High	287	8 (2.8)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 14-22. Analysis of Carotid Bruits (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
817	0.94 (0.65,1.36)	0.755

[a] Relative risk for a twofold increase in 1987 dioxin.

14.2.2.3.3 Radial Pulses

The unadjusted and adjusted Model 1 analyses of radial pulses were nonsignificant (Table 14-23(a,b): p>0.11 for each contrast).

Table 14-23. Analysis of Radial Pulses

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***7 (0.8)***	***2.52 (0.74,8.64)***	***0.131***
	Comparison	***1,232***	***4 (0.3)***		
Officer	Ranch Hand	334	2 (0.6)	1.45 (0.20,10.36)	0.710
	Comparison	484	2 (0.4)		
Enlisted Flyer	Ranch Hand	149	0 (0.0)	--	--
	Comparison	186	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	376	5 (1.3)	3.77 (0.73,19.55)	0.114
	Comparison	562	2 (0.4)		

--: Results not presented because of the sparse number of participants with an abnormal radial pulse.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***2.85 (0.67,12.16)***	***0.143***
Officer	1.24 (0.16,9.95)	0.837
Enlisted Flyer	--	--
Enlisted Groundcrew	5.69 (0.54,60.05)	0.148

--: Results not presented because of the sparse number of participants with an abnormal radial pulse.

Note: Results for all occupations combined are not adjusted for occupation because of the sparse number of participants with an abnormal radial pulse.

Table 14-23. Analysis of Radial Pulses (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	155	2 (1.3)	0.58 (0.17,1.99)	0.334
Medium	161	0 (0.0)		
High	160	1 (0.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)	p-Value
--	--	--

--: Results not presented because of the sparse number of Ranch Hands with an abnormal radial pulse.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,195	4 (0.3)		
Background RH	376	4 (1.1)	2.78 (0.69,11.27)	0.153
Low RH	233	2 (0.9)	2.64 (0.48,14.54)	0.264
High RH	243	1 (0.4)	1.41 (0.16,12.80)	0.759
Low plus High RH	476	3 (0.6)	1.92 (0.40,9.18)	0.414

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 14-23. Analysis of Radial Pulses (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Comparison	1,155		
Background RH	360	3.27 (0.64,16.71)	0.155
Low RH	221	3.82 (0.53,27.51)	0.183
High RH	236	1.26 (0.11,14.89)	0.856
Low plus High RH	457	2.15 (0.36,13.04)	0.404

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for occupation because of the sparse number of participants with an abnormal radial pulse.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**	
1987 Dioxin	**n**	**Number (%) Abnormal**	**Estimated Relative Risk (95% C.I.)[a]**	**p-Value**
Low	284	2 (0.7)	0.75 (0.43,1.32)	0.305
Medium	281	4 (1.4)		
High	287	1 (0.3)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
Analysis Results for Log_2 (1987 Dioxin + 1)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
817	0.61 (0.30,1.21)	0.140

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for occupation because of the sparse number of Ranch Hands with an abnormal radial pulse.

The unadjusted Model 2 analysis showed no significant association between radial pulses and initial dioxin (Table 14-23(c): p=0.334). Because of the sparse number of Ranch Hands with abnormal radial pulses, the adjusted Model 2 analysis was not performed.

All Model 3 and 4 analyses of radial pulses were nonsignificant (Table 14-23(e–h): p≥0.14 for each analysis).

14.2.2.3.4 Femoral Pulses

The unadjusted Model 1 analysis of femoral pulses revealed a marginally significant overall group difference between Ranch Hands and Comparisons (Table 14-24(a): Est. RR=1.83, p=0.080). Stratifying by occupation did not reveal any significant difference between Ranch Hands and Comparisons within each occupational stratum (Table 14-24(a): p>0.12 for each contrast). The percentage of participants with abnormal femoral pulses was greater for the Ranch Hands (2.2%) than for Comparisons (1.2%). The adjusted analysis did not show a significant difference between Ranch Hands and Comparisons over all occupations or within each occupational stratum (Table 14-24(b): p>0.17 for each contrast).

Table 14-24. Analysis of Femoral Pulses

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***19 (2.2)***	***1.83 (0.93,3.63)***	***0.080***
	Comparison	***1,231***	***15 (1.2)***		
Officer	Ranch Hand	334	7 (2.1)	1.27 (0.46,3.55)	0.643
	Comparison	484	8 (1.7)		
Enlisted Flyer	Ranch Hand	149	5 (3.4)	2.11 (0.50,8.96)	0.313
	Comparison	185	3 (1.6)		
Enlisted Groundcrew	Ranch Hand	376	7 (1.9)	2.65 (0.77,9.10)	0.123
	Comparison	562	4 (0.7)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.66 (0.79,3.49)***	***0.178***
Officer	1.51 (0.52,4.38)	0.448
Enlisted Flyer	1.48 (0.27,8.02)	0.652
Enlisted Groundcrew	2.08 (0.55,7.87)	0.282

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	155	3 (1.9)	0.97 (0.61,1.53)	0.890
Medium	161	5 (3.1)		
High	160	4 (2.5)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 14-24. Analysis of Femoral Pulses (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
457	1.17 (0.61,2.24)	0.641

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race because of the sparse number of participants with an abnormal femoral pulse.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,194	15 (1.3)		
Background RH	376	7 (1.9)	1.39 (0.56,3.45)	0.481
Low RH	233	6 (2.6)	2.10 (0.81,5.48)	0.128
High RH	243	6 (2.5)	2.13 (0.81,5.56)	0.125
Low plus High RH	476	12 (2.5)	2.11 (0.98,4.56)	0.056

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,154		
Background RH	360	1.22 (0.44,3.36)	0.702
Low RH	221	1.71 (0.58,4.98)	0.329
High RH	236	2.45 (0.76,7.90)	0.134
Low plus High RH	457	2.06 (0.85,4.96)	0.108

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 14-24. Analysis of Femoral Pulses (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	284	5 (1.8)	1.01 (0.75,1.38)	0.927
Medium	281	5 (1.8)		
High	287	9 (3.1)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
817	1.29 (0.83,2.03)	0.255

[a] Relative risk for a twofold increase in 1987 dioxin.

The Model 2 analyses did not reveal a significant association between femoral pulses and initial dioxin in either the unadjusted or adjusted analyses (Table 14-24(c,d): p>0.64 for each analysis).

The unadjusted Model 3 analysis showed a marginally significant difference between Ranch Hands in the low plus high dioxin category and Comparisons (Table 14-24(e): Est. RR=2.11, p=0.056). The percentage of abnormal femoral pulses for Ranch Hands in the low plus high dioxin category was 2.5 versus 1.3 percent for Comparisons. The adjusted analysis did not find any contrasts to be significant (Table 14-24(f): p>0.10 for each contrast).

The unadjusted and adjusted Model 4 analyses did not show a significant association between 1987 dioxin and femoral pulses (Table 14-24(g,h): p>0.25 for each analysis).

14.2.2.3.5 Popliteal Pulses

All unadjusted and adjusted Model 1 through 4 analyses were not significant (Table 14-25(a–h): p≥0.41 for each analysis).

Table 14-25. Analysis of Popliteal Pulses

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***23 (2.7)***	***1.18 (0.68,2.06)***	***0.561***
	Comparison	***1,230***	***28 (2.3)***		
Officer	Ranch Hand	334	7 (2.1)	0.84 (0.33,2.16)	0.717
	Comparison	483	12 (2.5)		
Enlisted Flyer	Ranch Hand	149	5 (3.4)	1.57 (0.41,5.96)	0.506
	Comparison	185	4 (2.2)		
Enlisted Groundcrew	Ranch Hand	376	11 (2.9)	1.38 (0.60,3.16)	0.445
	Comparison	562	12 (2.1)		

Table 14-25. Analysis of Popliteal Pulses (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.04 (0.56,1.90)***	***0.911***
Officer	0.95 (0.35,2.52)	0.911
Enlisted Flyer	0.99 (0.21,4.82)	0.995
Enlisted Groundcrew	1.13 (0.46,2.79)	0.784

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	155	4 (2.6)	0.89 (0.57,1.38)	0.601
Medium	161	6 (3.7)		
High	160	4 (2.5)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
457	0.97 (0.53,1.78)	0.924

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race because of the sparse number of Ranch Hands with an abnormal popliteal pulse.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,193	28 (2.3)		
Background RH	376	9 (2.4)	0.94 (0.44,2.03)	0.879
Low RH	233	7 (3.0)	1.31 (0.56,3.03)	0.535
High RH	243	7 (2.9)	1.33 (0.57,3.08)	0.512
Low plus High RH	476	14 (2.9)	1.32 (0.69,2.53)	0.410

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 14-25. Analysis of Popliteal Pulses (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Comparison	1,153		
Background RH	360	0.88 (0.37,2.05)	0.760
Low RH	221	1.15 (0.45,2.92)	0.776
High RH	236	1.08 (0.40,2.86)	0.884
Low plus High RH	457	1.11 (0.53,2.30)	0.781

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**	
1987 Dioxin	**n**	**Number (%) Abnormal**	**Estimated Relative Risk (95% C.I.)[a]**	**p-Value**
Low	284	6 (2.1)	0.98 (0.74,1.30)	0.891
Medium	281	7 (2.5)		
High	287	10 (3.5)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
817	1.02 (0.72,1.46)	0.908

[a] Relative risk for a twofold increase in 1987 dioxin.

14.2.2.3.6 Dorsalis Pedis Pulses

All unadjusted and adjusted analyses of dorsalis pedis pulses were nonsignificant (Table 14-26(a–h): p>0.11 for each analysis).

Table 14-26. Analysis of Dorsalis Pedis Pulses

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***69 (8.0)***	***1.04 (0.76,1.44)***	***0.796***
	Comparison	***1,230***	***95 (7.7)***		
Officer	Ranch Hand	334	27 (8.1)	1.24 (0.73,2.11)	0.429
	Comparison	483	32 (6.6)		
Enlisted Flyer	Ranch Hand	149	18 (12.1)	1.36 (0.67,2.74)	0.392
	Comparison	185	17 (9.2)		
Enlisted Groundcrew	Ranch Hand	376	24 (6.4)	0.76 (0.46,1.28)	0.305
	Comparison	562	46 (8.2)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.97 (0.69,1.37)***	***0.857***
Officer	1.27 (0.73,2.22)	0.398
Enlisted Flyer	1.33 (0.62,2.86)	0.463
Enlisted Groundcrew	0.64 (0.37,1.12)	0.117

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	155	12 (7.7)	0.90 (0.69,1.17)	0.417
Medium	161	16 (9.9)		
High	160	12 (7.5)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
457	1.11 (0.78,1.57)	0.561

[a] Relative risk for a twofold increase in initial dioxin.

Table 14-26. Analysis of Dorsalis Pedis Pulses (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,193	95 (8.0)		
Background RH	376	29 (7.7)	0.91 (0.59,1.40)	0.664
Low RH	233	22 (9.4)	1.22 (0.75,1.98)	0.429
High RH	243	18 (7.4)	0.98 (0.58,1.65)	0.931
Low plus High RH	476	40 (8.4)	1.09 (0.74,1.61)	0.670

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,153		
Background RH	360	0.94 (0.59,1.50)	0.792
Low RH	221	0.99 (0.58,1.70)	0.977
High RH	236	0.89 (0.50,1.58)	0.685
Low plus High RH	457	0.94 (0.61,1.43)	0.761

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	284	21 (7.4)	0.99 (0.84,1.17)	0.913
Medium	281	25 (8.9)		
High	287	23 (8.0)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 14-26. Analysis of Dorsalis Pedis Pulses (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
817	1.07 (0.85,1.33)	0.580

[a] Relative risk for a twofold increase in 1987 dioxin.

14.2.2.3.7 Posterior Tibial Pulses

All unadjusted and adjusted Models 1 through 4 analyses of posterior tibial pulses were nonsignificant (Table 14-27(a–h): p>0.11 for each analysis).

Table 14-27. Analysis of Posterior Tibial Pulses

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***58 (6.8)***	***1.32 (0.91,1.90)***	***0.142***
	Comparison	***1,228***	***64 (5.2)***		
Officer	Ranch Hand	334	22 (6.6)	1.41 (0.77,2.57)	0.263
	Comparison	483	23 (4.8)		
Enlisted Flyer	Ranch Hand	149	14 (9.4)	1.36 (0.62,2.98)	0.449
	Comparison	183	13 (7.1)		
Enlisted Groundcrew	Ranch Hand	376	22 (5.9)	1.19 (0.67,2.10)	0.562
	Comparison	562	28 (5.0)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.25 (0.84,1.86)***	***0.280***
Officer	1.40 (0.73,2.68)	0.307
Enlisted Flyer	1.17 (0.49,2.78)	0.724
Enlisted Groundcrew	1.16 (0.62,2.16)	0.649

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	155	9 (5.8)	1.01 (0.77,1.33)	0.925
Medium	161	15 (9.3)		
High	160	10 (6.3)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 14-27. Analysis of Posterior Tibial Pulses (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
457	1.16 (0.81,1.65)	0.417

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,191	63 (5.3)		
Background RH	376	22 (5.9)	1.04 (0.63,1.73)	0.865
Low RH	233	18 (7.7)	1.52 (0.88,2.61)	0.135
High RH	243	16 (6.6)	1.34 (0.76,2.36)	0.320
Low plus High RH	476	34 (7.1)	1.42 (0.92,2.19)	0.113

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,151		
Background RH	360	1.08 (0.62,1.89)	0.784
Low RH	221	1.31 (0.71,2.39)	0.387
High RH	236	1.21 (0.63,2.30)	0.571
Low plus High RH	457	1.25 (0.77,2.03)	0.358

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 14-27. Analysis of Posterior Tibial Pulses (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	284	18 (6.3)	1.03 (0.86,1.24)	0.746
Medium	281	16 (5.7)		
High	287	22 (7.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
817	1.12 (0.88,1.43)	0.354

[a] Relative risk for a twofold increase in 1987 dioxin.

14.2.2.3.8 Leg Pulses

Leg pulses were not significantly associated with dioxin in any of the unadjusted and adjusted Models 1 through 4 analyses (Table 14-28(a–h): p>0.15 for each analysis).

Table 14-28. Analysis of Leg Pulses

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***94 (10.9)***	***1.10 (0.83,1.47)***	***0.496***
	Comparison	***1,228***	***123 (10.0)***		
Officer	Ranch Hand	334	36 (10.8)	1.34 (0.83,2.15)	0.228
	Comparison	483	40 (8.3)		
Enlisted Flyer	Ranch Hand	149	25 (16.8)	1.48 (0.79,2.74)	0.218
	Comparison	183	22 (12.0)		
Enlisted Groundcrew	Ranch Hand	376	33 (8.8)	0.79 (0.51,1.23)	0.300
	Comparison	562	61 (10.9)		

Table 14-28. Analysis of Leg Pulses (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.03 (0.76,1.40)***	***0.850***
Officer	1.30 (0.79,2.16)	0.306
Enlisted Flyer	1.46 (0.74,2.88)	0.270
Enlisted Groundcrew	0.71 (0.44,1.14)	0.158

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	155	15 (9.7)	0.96 (0.77,1.20)	0.739
Medium	161	22 (13.7)		
High	160	16 (10.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
457	1.13 (0.84,1.51)	0.433

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,191	122 (10.2)		
Background RH	376	39 (10.4)	0.95 (0.65,1.40)	0.812
Low RH	233	29 (12.4)	1.26 (0.82,1.94)	0.298
High RH	243	24 (9.9)	1.01 (0.64,1.61)	0.957
Low plus High RH	476	53 (11.1)	1.13 (0.80,1.59)	0.498

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 14-28. Analysis of Leg Pulses (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,151		
Background RH	360	1.01 (0.66,1.53)	0.981
Low RH	221	1.01 (0.63,1.64)	0.955
High RH	236	0.91 (0.54,1.53)	0.725
Low plus High RH	457	0.96 (0.66,1.40)	0.832

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	284	30 (10.6)	1.00 (0.87,1.16)	0.956
Medium	281	31 (11.0)		
High	287	31 (10.8)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
817	1.08 (0.88,1.31)	0.467

[a] Relative risk for a twofold increase in 1987 dioxin.

14.2.2.3.9 Peripheral Pulses

All unadjusted and adjusted analyses in Models 1 through 4 were nonsignificant (Table 14–29(a–h): p>0.21 for each analysis).

Table 14-29. Analysis of Peripheral Pulses

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***97 (11.3)***	***1.11 (0.84,1.47)***	***0.454***
	Comparison	***1,228***	***126 (10.3)***		
Officer	Ranch Hand	334	37 (11.1)	1.31 (0.82,2.08)	0.258
	Comparison	483	42 (8.7)		
Enlisted Flyer	Ranch Hand	149	25 (16.8)	1.48 (0.79,2.74)	0.218
	Comparison	183	22 (12.0)		
Enlisted Groundcrew	Ranch Hand	376	35 (9.3)	0.83 (0.53,1.28)	0.396
	Comparison	562	62 (11.0)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.05 (0.77,1.42)***	***0.761***
Officer	1.27 (0.77,2.09)	0.353
Enlisted Flyer	1.48 (0.75,2.92)	0.260
Enlisted Groundcrew	0.75 (0.47,1.21)	0.242

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	155	16 (10.3)	0.96 (0.77,1.19)	0.703
Medium	161	22 (13.7)		
High	160	17 (10.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
457	1.06 (0.79,1.41)	0.718

[a] Relative risk for a twofold increase in initial dioxin.

Table 14-29. Analysis of Peripheral Pulses (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	**n**	**Number (%) Abnormal**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,191	125 (10.5)		
Background RH	376	40 (10.6)	0.95 (0.65,1.39)	0.797
Low RH	233	30 (12.9)	1.27 (0.83,1.95)	0.266
High RH	243	25 (10.3)	1.04 (0.66,1.63)	0.880
Low plus High RH	476	55 (11.6)	1.15 (0.82,1.61)	0.431

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Comparison	1,151		
Background RH	360	1.00 (0.66,1.52)	0.997
Low RH	221	1.05 (0.65,1.70)	0.833
High RH	236	0.94 (0.57,1.57)	0.828
Low plus High RH	457	1.00 (0.68,1.45)	0.981

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**	
1987 Dioxin	**n**	**Number (%) Abnormal**	**Estimated Relative Risk (95% C.I.)[a]**	**p-Value**
Low	284	31 (10.9)	1.00 (0.86,1.15)	0.972
Medium	281	32 (11.4)		
High	287	32 (11.1)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 14-29. Analysis of Peripheral Pulses (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
817	1.07 (0.88,1.30)	0.485

[a] Relative risk for a twofold increase in 1987 dioxin.

14.2.2.3.10 ICVI Index

The analysis of ICVI index did not show any significant associations with dioxin (Table 14-30(a–h): p>0.11 for each analysis).

Table 14-30. Analysis of ICVI Index

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***858***	***33 (3.8)***	***1.06 (0.67,1.67)***	***0.819***
	Comparison	***1,232***	***45 (3.7)***		
Officer	Ranch Hand	334	13 (3.9)	1.27 (0.59,2.70)	0.541
	Comparison	484	15 (3.1)		
Enlisted Flyer	Ranch Hand	149	7 (4.7)	0.71 (0.27,1.86)	0.492
	Comparison	186	12 (6.5)		
Enlisted Groundcrew	Ranch Hand	375	13 (3.5)	1.09 (0.53,2.24)	0.825
	Comparison	562	18 (3.2)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.99 (0.61,1.60)***	***0.958***
Officer	1.25 (0.57,2.70)	0.577
Enlisted Flyer	0.50 (0.17,1.51)	0.218
Enlisted Groundcrew	1.12 (0.53,2.39)	0.764

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	155	6 (3.9)	0.99 (0.71,1.37)	0.948
Medium	161	10 (6.2)		
High	160	7 (4.4)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 14-30. Analysis of ICVI Index (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
461	1.12 (0.73,1.72)	0.604

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for diabetic class because of the sparse number of Ranch Hands with an abnormal intermittent claudication and vascular insufficiency index.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,195	43 (3.6)		
Background RH	375	9 (2.4)	0.65 (0.31,1.35)	0.249
Low RH	233	9 (3.9)	1.08 (0.52,2.24)	0.839
High RH	243	14 (5.8)	1.66 (0.89,3.09)	0.112
Low plus High RH	476	23 (4.8)	1.34 (0.79,2.27)	0.272

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,155		
Background RH	360	0.69 (0.32,1.48)	0.340
Low RH	221	0.98 (0.46,2.11)	0.968
High RH	236	1.41 (0.69,2.89)	0.346
Low plus High RH	457	1.19 (0.67,2.09)	0.555

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 14-30. Analysis of ICVI Index (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	283	8 (2.8)	1.08 (0.86,1.37)	0.503
Medium	281	9 (3.2)		
High	287	15 (5.2)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
817	1.07 (0.79,1.45)	0.666

[a] Relative risk for a twofold increase in 1987 dioxin.

14.2.3 Longitudinal Analysis

Cardiovascular longitudinal analyses were conducted on systolic blood pressure measurements taken at the 1982 and 1997 examinations and six pulse assessments made at the 1985 and 1997 examinations. Discrete and continuous analyses were performed for systolic blood pressure. The six pulse measurements included femoral pulses, popliteal pulses, dorsalis pedis pulses, posterior tibial pulses, leg pulses, and peripheral pulses. The 1985 and 1997 measurements were used for the pulse assessments because the Doppler assessment of pulses was conducted at these two examinations and was not conducted at the 1982 baseline or 1987 follow-up examinations.

Longitudinal analyses were conducted to examine whether changes across time differed with respect to group membership (Model 1), initial dioxin (Model 2), and categorized dioxin (Model 3). Model 4 was not examined in longitudinal analyses because 1987 dioxin, the measure of exposure in these models, changes over time and is not available for all participants for 1982 or 1997.

Participants considered abnormal in 1982 (or 1985 for Doppler pulse measurements) were not included in the longitudinal analysis of discrete dependent variables. The purpose of the longitudinal analysis was to examine the effects of dioxin exposure across time. Participants who were abnormal in 1982 (or 1988) were not considered to be at risk for developing the condition, because the condition already existed at the time of the first collection of data for the AFHS (1982). Only participants who were normal at the 1982 (or 1985) examination were considered to be at risk for developing the condition; therefore, the rate of abnormalities under this restriction approximates an incidence rate between 1982 (or 1985) and 1997. That is, an incidence rate is a measure of the rate at which people without a condition develop the condition during a specified period of time (53). Summary statistics are provided for reference purposes for the 1985, 1987, and 1992 examinations for systolic blood pressure and for the 1992 examination for the pulse measurements.

The longitudinal analysis for systolic blood pressure in its discrete form examined relative risks at the 1997 examination for participants who were classified as normal at the 1982 examination. The longitudinal analysis for the Doppler pulse measurements examined relative risks at the 1997 examination for participants who were classified as normal at the 1985 examination. The adjusted relative risks estimated from each of the three models were used to investigate the change in the dependent variable over time. All three models were adjusted for age; Models 2 and 3 also were adjusted for the percentage of body fat at the time of the blood measurement of dioxin.

The longitudinal analysis for the systolic blood pressure in its continuous form examined the paired difference between the measurements from 1982 and 1997. These paired differences measured the change in systolic blood pressure over time. Each of the three models used in the longitudinal analysis was adjusted for age and systolic blood pressure as measured in 1982 (see Chapter 7, Statistical Methods).

14.2.3.1 Physical Examination Variables

14.2.3.1.1 Systolic Blood Pressure (Continuous)

The Model 1 analysis of change in mean systolic blood pressure revealed a marginally significant difference between overall Ranch Hands and Comparisons (Table 14-31(a): difference of examination mean change=–1.6 mm Hg, p=0.066). The Ranch Hand mean decreased by 6.3 mm Hg between 1982 and 1997, and the Comparison mean decreased by 4.7 mm Hg. Stratifying by occupation showed a marginally significant group difference in the enlisted groundcrew stratum (Table 14-31(a): difference of examination mean change=–2.2 mm Hg, p=0.079). For the enlisted groundcrew, the Ranch Hand mean decreased by 7.4 mm Hg between 1982 and 1997, and the Comparison mean decreased by 5.2 mm Hg.

Table 14-31. Longitudinal Analysis of Systolic Blood Pressure (mm Hg) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS										
		Mean[a]/(n) Examination								
Occupational Category	Group	1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	***Ranch Hand***	***131.1 (808)***	***117.8 (790)***	***125.9 (782)***	***120.4 (785)***	***124.8 (808)***	***–6.3***	***–1.6***	***0.066***
	Comparison	***130.7 (959)***	***118.9 (940)***	***126.4 (935)***	***121.3 (939)***	***126.0 (959)***	***–4.7***		
Officer	Ranch Hand	131.8 (305)	118.8 (301)	126.5 (298)	122.6 (300)	126.1 (305)	–5.6	–0.3	0.840
	Comparison	131.3 (372)	118.8 (365)	126.3 (360)	121.8 (367)	126.1 (372)	–5.3		
Enlisted Flyer	Ranch Hand	131.8 (146)	118.4 (143)	127.2 (141)	120.6 (142)	126.7 (146)	–5.1	–3.8	0.135
	Comparison	130.2 (144)	118.9 (143)	125.9 (142)	121.2 (142)	128.9 (144)	–1.3		
Enlisted Groundcrew	Ranch Hand	130.3 (357)	116.8 (346)	124.8 (343)	118.4 (343)	122.9 (357)	–7.4	–2.2	0.079
	Comparison	130.3 (443)	119.0 (432)	126.7 (433)	120.9 (430)	125.1 (443)	–5.2		

[a] Transformed from natural logarithm scale.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of natural logarithm of systolic blood pressure; results adjusted for natural logarithm of systolic blood pressure in 1982 and age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

Table 14-31. Longitudinal Analysis of Systolic Blood Pressure (mm Hg) (Continuous) (Continued)

(b) MODEL 2: RANCH HANDS – INITIAL DIOXIN							
Initial Dioxin Category Summary Statistics						Analysis Results for Log_2 (Initial Dioxin)[b]	
	Mean[a]/(n) Examination						
Initial Dioxin	1982	1985	1987	1992	1997	Adjusted Slope (Std. Error)	p-Value
Low	132.2 (149)	118.4 (146)	127.1 (148)	120.5 (144)	125.9 (149)	0.000 (0.005)	0.977
Medium	132.8 (158)	119.7 (155)	126.4 (155)	122.9 (155)	125.5 (158)		
High	131.2 (153)	119.1 (150)	127.4 (148)	121.1 (150)	124.1 (153)		

[a] Transformed from natural logarithm scale.
[b] Results based on difference between natural logarithm of 1997 systolic blood pressure and natural logarithm of 1982 systolic blood pressure versus $\log_2$ (initial dioxin); results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of 1982 systolic blood pressure, and age in 1997.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

Table 14-31. Longitudinal Analysis of Systolic Blood Pressure (mm Hg) (Continuous) (Continued)

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY								
	Mean[a]/(n) Examination							
Dioxin Category	1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
Comparison	130.6 (932)	118.7 (916)	126.2 (910)	121.1 (913)	126.0 (932)	–4.7		
Background RH	129.8 (342)	116.2 (334)	124.4 (326)	119.0 (331)	124.4 (342)	–5.3	–0.6	0.386
Low RH	132.0 (224)	118.7 (218)	126.8 (221)	120.9 (217)	126.0 (224)	–6.0	–1.3	0.347
High RH	132.1 (236)	119.5 (233)	127.2 (230)	122.0 (232)	124.4 (236)	–7.8	–3.1	0.086
Low plus High RH	132.1 (460)	119.1 (451)	127.0 (451)	121.5 (449)	125.2 (460)	–6.9	–2.2	0.083

[a] Transformed from natural logarithm scale.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of natural logarithm of 1997 systolic blood pressure; results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of 1982 systolic blood pressure, and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

The longitudinal analysis in Model 2 did not reveal a significant association between the change in mean systolic blood pressure and dioxin (Table 14-31(b): p=0.977).

The Model 3 analysis of the change in mean systolic blood pressure levels between 1982 and 1997 revealed two marginally significant contrasts: Ranch Hands in the high dioxin category versus Comparisons (Table 14-31(c): difference of examination mean change=–3.1 mm Hg, p=0.086) and Ranch Hands in the low plus high dioxin category versus Comparisons (Table 14-31(c): difference of examination mean change=–2.2 mm Hg, p=0.083). The change in means between 1982 and 1997 for Ranch Hands in the high dioxin category, Ranch Hands in the low plus high dioxin category, and Comparisons was –7.8 mm Hg, –6.9 mm Hg, and –4.7 mm Hg, respectively.

14.2.3.1.2 Systolic Blood Pressure (Discrete)

The longitudinal analysis in Models 1 through 3 did not reveal a significant association between dioxin and change in systolic blood pressure in its discrete form (Table 14-32(a–c): p>0.45 for each analysis).

Table 14-32. Longitudinal Analysis of Systolic Blood Pressure (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) High/(n) Examination				
		1982	1985	1987	1992	1997
All	***Ranch Hand***	***141 (17.5) (808)***	***42 (5.3) (790)***	***146 (18.7) (782)***	***119 (15.2) (785)***	***169 (20.9) (808)***
	Comparison	***187 (19.5) (959)***	***65 (6.9) (940)***	***205 (21.9) (935)***	***146 (15.5) (939)***	***215 (22.4) (959)***
Officer	Ranch Hand	60 (19.7) (305)	20 (6.6) (301)	59 (19.8) (298)	51 (17.0) (300)	73 (23.9) (305)
	Comparison	75 (20.2) (372)	25 (6.8) (365)	81 (22.5) (360)	65 (17.7) (367)	90 (24.2) (372)
Enlisted Flyer	Ranch Hand	28 (19.2) (146)	5 (3.5) (143)	29 (20.6) (141)	23 (16.2) (142)	35 (24.0) (146)
	Comparison	27 (18.8) (144)	11 (7.7) (143)	31 (21.8) (142)	20 (14.1) (142)	38 (26.4) (144)
Enlisted Groundcrew	Ranch Hand	53 (14.8) (357)	17 (4.9) (346)	58 (16.9) (343)	45 (13.1) (343)	61 (17.1) (357)
	Comparison	85 (19.2) (443)	29 (6.7) (432)	93 (21.5) (433)	61 (14.2) (430)	87 (19.6) (443)

Occupational Category	Group	Normal in 1982: n in 1997	Normal in 1982: Number (%) High in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***667***	***111 (16.6)***	***0.99 (0.75,1.31)***	***0.951***
	Comparison	***772***	***130 (16.8)***		
Officer	Ranch Hand	245	48 (19.6)	1.18 (0.76,1.84)	0.454
	Comparison	297	50 (16.8)		
Enlisted Flyer	Ranch Hand	118	23 (19.5)	0.90 (0.47,1.71)	0.743
	Comparison	117	25 (21.4)		
Enlisted Groundcrew	Ranch Hand	304	40 (13.2)	0.86 (0.55,1.35)	0.513
	Comparison	358	55 (15.4)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had normal systolic blood pressure in 1982 (see Chapter 7, Statistical Methods).

Table 14-32. Longitudinal Analysis of Systolic Blood Pressure (Discrete) (Continued)

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN					
	Number (%) High/(n) Examination				
Initial Dioxin	1982	1985	1987	1992	1997
Low	32 (21.5) (149)	6 (4.1) (146)	33 (22.3) (148)	24 (16.7) (144)	37 (24.8) (149)
Medium	32 (20.3) (158)	8 (5.2) (155)	28 (18.1) (155)	28 (18.1) (155)	34 (21.5) (158)
High	22 (14.4) (153)	11 (7.3) (150)	30 (20.3) (148)	25 (16.7) (150)	28 (18.3) (153)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1982			
Initial Dioxin	n in 1997	Number (%) High in 1997	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	117	22 (18.8)	0.96 (0.78,1.19)	0.714
Medium	126	23 (18.3)		
High	131	20 (15.3)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had normal systolic blood pressure in 1982 (see Chapter 7, Statistical Methods).

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY					
	Number (%) High/(n) Examination				
Dioxin Category	1982	1985	1987	1992	1997
Comparison	180 (19.3) (932)	60 (6.6) (916)	194 (21.3) (910)	140 (15.3) (913)	207 (22.2) (932)
Background RH	54 (15.8) (342)	17 (5.1) (334)	54 (16.6) (326)	42 (12.7) (331)	69 (20.2) (342)
Low RH	43 (19.2) (224)	8 (3.7) (218)	44 (19.9) (221)	35 (16.1) (217)	54 (24.1) (224)
High RH	43 (18.2) (236)	17 (7.3) (233)	47 (20.4) (230)	42 (18.1) (232)	45 (19.1) (236)
Low plus High RH	86 (18.7) (460)	25 (5.5) (451)	91 (20.2) (451)	77 (17.1) (449)	99 (21.5) (460)

Table 14-32. Longitudinal Analysis of Systolic Blood Pressure (Discrete) (Continued)

	Normal in 1982			
Dioxin Category	n in 1997	Number (%) High in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	752	127 (16.9)		
Background RH	288	45 (15.6)	0.96 (0.66,1.41)	0.840
Low RH	181	34 (18.8)	1.01 (0.65,1.55)	0.978
High RH	193	31 (16.1)	1.01 (0.65,1.57)	0.965
Low plus High RH	374	65 (17.4)	1.01 (0.72,1.41)	0.963

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had normal systolic blood pressure in 1982 (see Chapter 7, Statistical Methods).

14.2.3.1.3 Femoral Pulses

The Model 1 analysis of the change in percentage of abnormal femoral pulses did not reveal a significant difference between Ranch Hands and Comparisons overall (Table 14-33(a): p=0.118). Stratifying by occupation showed a marginally significant group difference in the enlisted groundcrew stratum (Table 14-33(a): Adj. RR=3.19, p=0.095). For enlisted groundcrew, 1.9 percent of the Ranch Hands and 0.6 percent of the Comparisons had normal femoral pulses in 1985 and abnormal femoral pulses in 1997.

The Model 2 longitudinal analysis revealed no significant association between dioxin and the percentage of participants with normal femoral pulses in 1985 and abnormal femoral pulses in 1997 (Table 14-33(b): p=0.972).

Table 14-33. Longitudinal Analysis of Femoral Pulses

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) Abnormal/(n) Examination 1985	1992	1997
All	***Ranch Hand***	***0 (0.0) (823)***	***6 (0.7) (802)***	***19 (2.3) (823)***
	Comparison	***0 (0.0) (1,047)***	***6 (0.6) (1,020)***	***14 (1.3) (1,047)***
Officer	Ranch Hand	0 (0.0) (318)	4 (1.3) (313)	7 (2.2) (318)
	Comparison	0 (0.0) (412)	2 (0.5) (405)	8 (1.9) (412)
Enlisted Flyer	Ranch Hand	0 (0.0) (145)	0 (0.0) (143)	5 (3.4) (145)
	Comparison	0 (0.0) (158)	2 (1.3) (156)	3 (1.9) (158)
Enlisted Groundcrew	Ranch Hand	0 (0.0) (360)	2 (0.6) (346)	7 (1.9) (360)
	Comparison	0 (0.0) (477)	2 (0.4) (459)	3 (0.6) (477)

Occupational Category	Group	Normal in 1985: n in 1997	Number (%) Abnormal in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***823***	***19 (2.3)***	***1.74 (0.86,3.49)***	***0.118***
	Comparison	***1,047***	***14 (1.3)***		
Officer	Ranch Hand	318	7 (2.2)	1.12 (0.40,3.13)	0.824
	Comparison	412	8 (1.9)		
Enlisted Flyer	Ranch Hand	145	5 (3.4)	1.82 (0.43,7.77)	0.419
	Comparison	158	3 (1.9)		
Enlisted Groundcrew	Ranch Hand	360	7 (1.9)	3.19 (0.82,12.42)	0.095
	Comparison	477	3 (0.6)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1985 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1992 are provided for reference purposes for participants who attended the 1985 and 1997 examinations. Statistical analyses are based only on participants who had normal femoral pulses in 1985 (see Chapter 7, Statistical Methods).

Table 14-33. Longitudinal Analysis of Femoral Pulses (Continued)

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN			
	Number (%) Abnormal/(n) Examination		
Initial Dioxin	1985	1992	1997
Low	0 (0.0) (149)	3 (2.1) (144)	3 (2.0) (149)
Medium	0 (0.0) (158)	1 (0.6) (155)	5 (3.2) (158)
High	0 (0.0) (155)	0 (0.0) (151)	4 (2.6) (155)

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)[a]	
	Normal in 1985			
Initial Dioxin	n in 1997	Number (%) Abnormal in 1997	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	149	3 (2.0)	1.01 (0.63,1.61)	0.972
Medium	158	5 (3.2)		
High	155	4 (2.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1992 are provided for reference purposes for participants who attended the 1985 and 1997 examinations. Statistical analyses are based only on participants who had normal femoral pulses in 1985 (see Chapter 7, Statistical Methods).

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY			
	Number (%) Abnormal/(n) Examination		
Dioxin Category	1985	1992	1997
Comparison	0 (0.0) (1,019)	6 (0.6) (994)	14 (1.4) (1,019)
Background RH	0 (0.0) (355)	2 (0.6) (346)	7 (2.0) (355)
Low RH	0 (0.0) (224)	4 (1.8) (217)	6 (2.7) (224)
High RH	0 (0.0) (238)	0 (0.0) (233)	6 (2.5) (238)
Low plus High RH	0 (0.0) (462)	4 (0.9) (450)	12 (2.6) (462)

Table 14-33. Longitudinal Analysis of Femoral Pulses (Continued)

Dioxin Category	Normal in 1985: n in 1997	Normal in 1985: Number (%) Abnormal in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	1,019	14 (1.4)		
Background RH	355	7 (2.0)	1.28 (0.51,3.21)	0.602
Low RH	224	6 (2.7)	1.88 (0.71,4.98)	0.202
High RH	238	6 (2.5)	2.34 (0.87,6.25)	0.091
Low plus High RH	462	12 (2.6)	2.10 (0.96,4.62)	0.063

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1992 are provided for reference purposes for participants who attended the 1985 and 1997 examinations. Statistical analyses are based only on participants who had normal femoral pulses in 1985 (see Chapter 7, Statistical Methods).

Model 3 analysis of the change in femoral pulses from normal in 1985 to abnormal in 1997 revealed two marginally significant contrasts: Ranch Hands in the high dioxin category versus Comparisons (Table 14-33(c): Adj. RR=2.34, p=0.091) and Ranch Hands in the low plus high dioxin category versus Comparisons (Table 14-33(c): Adj. RR=2.10, p=0.063). Of the Comparisons, 1.4 percent had normal femoral pulses in 1985 and abnormal femoral pulses in 1997. Of the Ranch Hands, 2.5 percent in the high dioxin category and 2.6 percent in the low plus high dioxin category had normal femoral pulses in 1985 and abnormal femoral pulses in 1997.

14.2.3.1.4 Popliteal Pulses

Analyses of Models 1 through 3 showed no significant associations between dioxin and the change in popliteal pulses between 1985 and 1997 (Table 14-34(a–c): p>0.19 for each analysis).

Table 14-34. Longitudinal Analysis of Popliteal Pulses

(a) MODEL 1: RANCH HANDS VS. COMPARISONS				
		Number (%) Abnormal/(n) Examination		
Occupational Category	Group	1985	1992	1997
All	***Ranch Hand***	***2 (0.2) (823)***	***10 (1.2) (802)***	***23 (2.8) (823)***
	Comparison	***1 (0.1) (1,046)***	***7 (0.7) (1,019)***	***24 (2.3) (1,046)***
Officer	Ranch Hand	1 (0.3) (318)	6 (1.9) (313)	7 (2.2) (318)
	Comparison	0 (0.0) (411)	4 (1.0) (404)	11 (2.7) (411)
Enlisted Flyer	Ranch Hand	0 (0.0) (145)	2 (1.4) (143)	5 (3.4) (145)
	Comparison	1 (0.6) (158)	2 (1.3) (156)	3 (1.9) (158)
Enlisted Groundcrew	Ranch Hand	1 (0.3) (360)	2 (0.6) (346)	11 (3.1) (360)
	Comparison	0 (0.0) (477)	1 (0.2) (459)	10 (2.1) (477)

		Normal in 1985			
Occupational Category	Group	n in 1997	Number (%) Abnormal in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***821***	***22 (2.7)***	***1.22 (0.67,2.21)***	***0.518***
	Comparison	***1,045***	***23 (2.2)***		
Officer	Ranch Hand	317	7 (2.2)	0.81 (0.31,2.13)	0.672
	Comparison	411	11 (2.7)		
Enlisted Flyer	Ranch Hand	145	5 (3.4)	2.67 (0.51,14.07)	0.246
	Comparison	157	2 (1.3)		
Enlisted Groundcrew	Ranch Hand	359	10 (2.8)	1.39 (0.57,3.40)	0.473
	Comparison	477	10 (2.1)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1985 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1992 are provided for reference purposes for participants who attended the 1985 and 1997 examinations. Statistical analyses are based only on participants who had normal popliteal pulses in 1985 (see Chapter 7, Statistical Methods).

Table 14-34. Longitudinal Analysis of Popliteal Pulses (Continued)

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN			
	Number (%) Abnormal/(n) Examination		
Initial Dioxin	1985	1992	1997
Low	0 (0.0) (149)	3 (2.1) (144)	4 (2.7) (149)
Medium	0 (0.0) (158)	2 (1.3) (155)	6 (3.8) (158)
High	0 (0.0) (155)	2 (1.3) (151)	4 (2.6) (155)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1985			
Initial Dioxin	n in 1997	Number (%) Abnormal in 1997	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	149	4 (2.7)	0.95 (0.61,1.49)	0.838
Medium	158	6 (3.8)		
High	155	4 (2.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1992 are provided for reference purposes for participants who attended the 1985 and 1997 examinations. Statistical analyses are based only on participants who had normal popliteal pulses in 1985 (see Chapter 7, Statistical Methods).

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY			
	Number (%) Abnormal/(n) Examination		
Dioxin Category	1985	1992	1997
Comparison	1 (0.1) (1,018)	7 (0.7) (993)	24 (2.4) (1,018)
Background RH	2 (0.6) (355)	3 (0.9) (346)	9 (2.5) (355)
Low RH	0 (0.0) (224)	4 (1.8) (217)	7 (3.1) (224)
High RH	0 (0.0) (238)	3 (1.3) (233)	7 (2.9) (238)
Low plus High RH	0 (0.0) (462)	7 (1.6) (450)	14 (3.0) (462)

Table 14-34. Longitudinal Analysis of Popliteal Pulses (Continued)

Dioxin Category	Normal in 1985: n in 1997	Normal in 1985: Number (%) Abnormal in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	1,017	23 (2.3)		
Background RH	353	8 (2.3)	0.87 (0.38,1.97)	0.731
Low RH	224	7 (3.1)	1.30 (0.55,3.09)	0.555
High RH	238	7 (2.9)	1.79 (0.75,4.30)	0.193
Low plus High RH	462	14 (3.0)	1.53 (0.77,3.03)	0.221

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1992 are provided for reference purposes for participants who attended the 1985 and 1997 examinations. Statistical analyses are based only on participants who had normal popliteal pulses in 1985 (see Chapter 7, Statistical Methods).

14.2.3.1.5 Dorsalis Pedis Pulses

The longitudinal analyses in Models 1 through 3 did not reveal any significant associations between dioxin and the change in dorsalis pedis pulses (Table 14-35(a–c): p>0.33 for each analysis).

Table 14-35. Longitudinal Analysis of Dorsalis Pedis Pulses

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) Abnormal/(n) Examination: 1985	1992	1997
All	***Ranch Hand***	***94 (11.4) (821)***	***60 (7.5) (798)***	***67 (8.2) (821)***
	Comparison	***111 (10.6) (1,044)***	***70 (6.9) (1,017)***	***85 (8.1) (1,044)***
Officer	Ranch Hand	41 (12.9) (318)	23 (7.4) (312)	27 (8.5) (318)
	Comparison	43 (10.5) (409)	28 (7.0) (402)	30 (7.3) (409)
Enlisted Flyer	Ranch Hand	16 (11.0) (145)	9 (6.3) (143)	18 (12.4) (145)
	Comparison	23 (14.6) (158)	16 (10.3) (156)	13 (8.2) (158)
Enlisted Groundcrew	Ranch Hand	37 (10.3) (358)	28 (8.2) (343)	22 (6.1) (358)
	Comparison	45 (9.4) (477)	26 (5.7) (459)	42 (8.8) (477)

Table 14-35. Longitudinal Analysis of Dorsalis Pedis Pulses (Continued)

Occupational Category	Group	Normal in 1985: n in 1997	Normal in 1985: Number (%) Abnormal in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***727***	***50 (6.9)***	***0.97 (0.66,1.43)***	***0.894***
	Comparison	***933***	***66 (7.1)***		
Officer	Ranch Hand	277	22 (7.9)	1.07 (0.59,1.93)	0.821
	Comparison	366	27 (7.4)		
Enlisted Flyer	Ranch Hand	129	12 (9.3)	1.42 (0.58,3.52)	0.444
	Comparison	135	9 (6.7)		
Enlisted Groundcrew	Ranch Hand	321	16 (5.0)	0.73 (0.39,1.38)	0.335
	Comparison	432	30 (6.9)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1985 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1992 are provided for reference purposes for participants who attended the 1985 and 1997 examinations. Statistical analyses are based only on participants who had normal dorsalis pedis pulses in 1985 (see Chapter 7, Statistical Methods).

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN

Initial Dioxin	Number (%) Abnormal/(n) Examination: 1985	1992	1997
Low	14 (9.4) (149)	8 (5.6) (144)	12 (8.1) (149)
Medium	20 (12.7) (158)	14 (9.0) (155)	16 (10.1) (158)
High	12 (7.8) (154)	9 (6.0) (149)	10 (6.5) (154)

Initial Dioxin	Initial Dioxin Category Summary Statistics — Normal in 1985: n in 1997	Number (%) Abnormal in 1997	Analysis Results for Log_2 (Initial Dioxin)[a]: Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	135	10 (7.4)	1.01 (0.72,1.41)	0.946
Medium	138	11 (8.0)		
High	142	7 (4.9)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1992 are provided for reference purposes for participants who attended the 1985 and 1997 examinations. Statistical analyses are based only on participants who had normal dorsalis pedis pulses in 1985 (see Chapter 7, Statistical Methods).

Table 14-35. Longitudinal Analysis of Dorsalis Pedis Pulses (Continued)

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY			
	Number (%) Abnormal/(n) Examination		
Dioxin Category	1985	1992	1997
Comparison	108 (10.6) (1,016)	70 (7.1) (991)	85 (8.4) (1,016)
Background RH	48 (13.5) (355)	29 (8.4) (345)	29 (8.2) (355)
Low RH	21 (9.4) (224)	12 (5.5) (217)	22 (9.8) (224)
High RH	25 (10.5) (237)	19 (8.2) (231)	16 (6.8) (237)
Low plus High RH	46 (10.0) (461)	31 (6.9) (448)	38 (8.2) (461)

	Normal in 1985			
Dioxin Category	n in 1997	Number (%) Abnormal in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	908	66 (7.3)		
Background RH	307	22 (7.2)	0.89 (0.53,1.48)	0.650
Low RH	203	17 (8.4)	1.08 (0.61,1.89)	0.798
High RH	212	11 (5.2)	0.91 (0.47,1.78)	0.789
Low plus High RH	415	28 (6.7)	0.99 (0.62,1.59)	0.964

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1992 are provided for reference purposes for participants who attended the 1985 and 1997 examinations. Statistical analyses are based only on participants who had normal dorsalis pedis pulses in 1985 (see Chapter 7, Statistical Methods).

14.2.3.1.6 Posterior Tibial Pulses

Model 1 and 2 analyses did not show any significant associations between dioxin and the change in posterior tibial pulses between 1985 and 1997 (Table 14-36(a,b): p>0.12 for each analysis).

Model 3 analysis of the change in posterior tibial pulses from normal in 1985 to abnormal in 1997 revealed one significant and one marginally significant contrast: Ranch Hands in the high dioxin category versus Comparisons (Table 14-36(c): Adj. RR=1.70, p=0.090) and Ranch Hands in the low plus high dioxin category versus Comparisons (Table 14-36(c): Adj. RR=1.60, p=0.047). Of the Comparisons, 5.1 percent had normal posterior tibial pulses in 1985 and abnormal posterior tibial pulses

in 1997. Of the Ranch Hands, 6.3 percent in the high dioxin category and 7.2 percent in the low plus high dioxin category had normal posterior tibial pulses in 1985 and abnormal posterior tibial pulses in 1997.

Table 14-36. Longitudinal Analysis of Posterior Tibial Pulses

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) Abnormal/(n) Examination 1985	1992	1997
All	***Ranch Hand***	***2 (0.2) (822)***	***20 (2.5) (801)***	***56 (6.8) (822)***
	Comparison	***6 (0.6) (1,044)***	***22 (2.2) (1,017)***	***58 (5.6) (1,044)***
Officer	Ranch Hand	1 (0.3) (318)	9 (2.9) (313)	21 (6.6) (318)
	Comparison	2 (0.5) (411)	10 (2.5) (404)	23 (5.6) (411)
Enlisted Flyer	Ranch Hand	1 (0.7) (145)	5 (3.5) (143)	14 (9.7) (145)
	Comparison	1 (0.6) (156)	4 (2.6) (154)	10 (6.4) (156)
Enlisted Groundcrew	Ranch Hand	0 (0.0) (359)	6 (1.7) (345)	21 (5.8) (359)
	Comparison	3 (0.6) (477)	8 (1.7) (459)	25 (5.2) (477)

Occupational Category	Group	Normal in 1985: n in 1997	Normal in 1985: Number (%) Abnormal in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***820***	***56 (6.8)***	***1.36 (0.92,2.01)***	***0.129***
	Comparison	***1,038***	***53 (5.1)***		
Officer	Ranch Hand	317	21 (6.6)	1.29 (0.69,2.43)	0.423
	Comparison	409	21 (5.1)		
Enlisted Flyer	Ranch Hand	144	14 (9.7)	1.70 (0.70,4.09)	0.239
	Comparison	155	9 (5.8)		
Enlisted Groundcrew	Ranch Hand	359	21 (5.8)	1.26 (0.68,2.35)	0.458
	Comparison	474	23 (4.9)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1985 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1992 are provided for reference purposes for participants who attended the 1985 and 1997 examinations. Statistical analyses are based only on participants who had normal posterior tibial pulses in 1985 (see Chapter 7, Statistical Methods).

Table 14-36. Longitudinal Analysis of Posterior Tibial Pulses (Continued)

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN

Initial Dioxin	Number (%) Abnormal/(n) Examination 1985	1992	1997
Low	1 (0.7) (149)	5 (3.5) (144)	9 (6.0) (149)
Medium	0 (0.0) (158)	5 (3.2) (155)	15 (9.5) (158)
High	1 (0.6) (155)	2 (1.3) (151)	9 (5.8) (155)

Initial Dioxin Category Summary Statistics: Initial Dioxin	Normal in 1985: n in 1997	Normal in 1985: Number (%) Abnormal in 1997	Analysis Results for Log_2 (Initial Dioxin)[a]: Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	148	9 (6.1)	1.12 (0.85,1.49)	0.418
Medium	158	15 (9.5)		
High	154	9 (5.8)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1992 are provided for reference purposes for participants who attended the 1985 and 1997 examinations. Statistical analyses are based only on participants who had normal posterior tibial pulses in 1985 (see Chapter 7, Statistical Methods).

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY

Dioxin Category	Number (%) Abnormal/(n) Examination 1985	1992	1997
Comparison	6 (0.6) (1,016)	22 (2.2) (991)	57 (5.6) (1,016)
Background RH	0 (0.0) (355)	7 (2.0) (346)	22 (6.2) (355)
Low RH	1 (0.4) (224)	6 (2.8) (217)	18 (8.0) (224)
High RH	1 (0.4) (238)	6 (2.6) (233)	15 (6.3) (238)
Low plus High RH	2 (0.4) (462)	12 (2.7) (450)	33 (7.1) (462)

Table 14-36. Longitudinal Analysis of Posterior Tibial Pulses (Continued)

Dioxin Category	Normal in 1985: n in 1997	Normal in 1985: Number (%) Abnormal in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	1,010	52 (5.1)		
Background RH	355	22 (6.2)	1.05 (0.62,1.77)	0.856
Low RH	223	18 (8.1)	1.50 (0.85,2.65)	0.160
High RH	237	15 (6.3)	1.70 (0.92,3.12)	0.090
Low plus High RH	460	33 (7.2)	1.60 (1.01,2.54)	0.047

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1992 are provided for reference purposes for participants who attended the 1985 and 1997 examinations. Statistical analyses are based only on participants who had normal posterior tibial pulses in 1985 (see Chapter 7, Statistical Methods).

14.2.3.1.7 Leg Pulses

The longitudinal analyses in Models 1 through 3 did not reveal a significant association between dioxin and the change from normal leg pulses in 1985 to abnormal leg pulses in 1997 (Table 14-37(a–c): p>0.15 for each analysis).

Table 14-37. Longitudinal Analysis of Leg Pulses

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) Abnormal/(n) Examination: 1985	1992	1997
All	***Ranch Hand***	***97 (11.8) (821)***	***66 (8.3) (798)***	***91 (11.1) (821)***
	Comparison	***114 (10.9) (1,042)***	***77 (7.6) (1,015)***	***109 (10.5) (1,042)***
Officer	Ranch Hand	43 (13.5) (318)	24 (7.7) (312)	35 (11.0) (318)
	Comparison	44 (10.8) (409)	29 (7.2) (402)	38 (9.3) (409)
Enlisted Flyer	Ranch Hand	17 (11.7) (145)	11 (7.7) (143)	25 (17.2) (145)
	Comparison	22 (14.1) (156)	16 (10.4) (154)	17 (10.9) (156)
Enlisted Groundcrew	Ranch Hand	37 (10.3) (358)	31 (9.0) (343)	31 (8.7) (358)
	Comparison	48 (10.1) (477)	32 (7.0) (459)	54 (11.3) (477)

Table 14-37. Longitudinal Analysis of Leg Pulses (Continued)

Occupational Category	Group	Normal in 1985: n in 1997	Normal in 1985: Number (%) Abnormal in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***724***	***73 (10.1)***	***1.12 (0.80,1.57)***	***0.502***
	Comparison	***928***	***85 (9.2)***		
Officer	Ranch Hand	275	29 (10.5)	1.13 (0.67,1.93)	0.645
	Comparison	365	34 (9.3)		
Enlisted Flyer	Ranch Hand	128	19 (14.8)	1.76 (0.81,3.83)	0.153
	Comparison	134	12 (9.0)		
Enlisted Groundcrew	Ranch Hand	321	25 (7.8)	0.89 (0.52,1.52)	0.676
	Comparison	429	39 (9.1)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1985 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1992 are provided for reference purposes for participants who attended the 1985 and 1997 examinations. Statistical analyses are based only on participants who had normal leg pulses in 1985 (see Chapter 7, Statistical Methods).

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN

Initial Dioxin	Number (%) Abnormal/(n) Examination: 1985	1992	1997
Low	15 (10.1) (149)	9 (6.3) (144)	15 (10.1) (149)
Medium	20 (12.7) (158)	17 (11.0) (155)	22 (13.9) (158)
High	13 (8.4) (154)	9 (6.0) (149)	14 (9.1) (154)

Initial Dioxin	Initial Dioxin Category Summary Statistics — Normal in 1985: n in 1997	Number (%) Abnormal in 1997	Analysis Results for Log$_2$ (Initial Dioxin)[a]: Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	134	13 (9.7)	1.14 (0.87,1.49)	0.344
Medium	138	17 (12.3)		
High	141	11 (7.8)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1992 are provided for reference purposes for participants who attended the 1985 and 1997 examinations. Statistical analyses are based only on participants who had normal leg pulses in 1985 (see Chapter 7, Statistical Methods).

Table 14-37. Longitudinal Analysis of Leg Pulses (Continued)

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY			
	Number (%) Abnormal/(n) Examination		
Dioxin Category	1985	1992	1997
Comparison	111 (10.9) (1,014)	77 (7.8) (989)	108 (10.7) (1,014)
Background RH	49 (13.8) (355)	30 (8.7) (345)	39 (11.0) (355)
Low RH	22 (9.8) (224)	13 (6.0) (217)	29 (12.9) (224)
High RH	26 (11.0) (237)	22 (9.5) (231)	22 (9.3) (237)
Low plus High RH	48 (10.4) (461)	35 (7.8) (448)	51 (11.1) (461)

	Normal in 1985			
Dioxin Category	n in 1997	Number (%) Abnormal in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	903	84 (9.3)		
Background RH	306	31 (10.1)	0.98 (0.63,1.52)	0.924
Low RH	202	24 (11.9)	1.21 (0.74,1.97)	0.455
High RH	211	17 (8.1)	1.17 (0.67,2.04)	0.589
Low plus High RH	413	41 (9.9)	1.19 (0.79,1.78)	0.411

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1992 are provided for reference purposes for participants who attended the 1985 and 1997 examinations. Statistical analyses are based only on participants who had normal leg pulses in 1985 (see Chapter 7, Statistical Methods).

14.2.3.1.8 Peripheral Pulses

The change from normal peripheral pulses in 1985 to abnormal peripheral pulses in 1997 was not significantly associated with dioxin in Models 1 through 3 (Table 14-38(a–c): p>0.15 for each analysis).

Table 14-38. Longitudinal Analysis of Peripheral Pulses

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) Abnormal/(n) Examination 1985	1992	1997
All	***Ranch Hand***	***97 (11.8) (821)***	***66 (8.3) (798)***	***94 (11.4) (821)***
	Comparison	***116 (11.1) (1,041)***	***81 (8.0) (1,014)***	***112 (10.8) (1,041)***
Officer	Ranch Hand	43 (13.5) (318)	24 (7.7) (312)	36 (11.3) (318)
	Comparison	44 (10.8) (409)	30 (7.5) (402)	40 (9.8) (409)
Enlisted Flyer	Ranch Hand	17 (11.7) (145)	11 (7.7) (143)	25 (17.2) (145)
	Comparison	22 (14.1) (156)	16 (10.4) (154)	17 (10.9) (156)
Enlisted Groundcrew	Ranch Hand	37 (10.3) (358)	31 (9.0) (343)	33 (9.2) (358)
	Comparison	50 (10.5) (476)	35 (7.6) (458)	55 (11.6) (476)

Occupational Category	Group	Normal in 1985: n in 1997	Number (%) Abnormal in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***724***	***76 (10.5)***	***1.14 (0.82,1.59)***	***0.433***
	Comparison	***925***	***87 (9.4)***		
Officer	Ranch Hand	275	30 (10.9)	1.10 (0.66,1.86)	0.710
	Comparison	365	36 (9.9)		
Enlisted Flyer	Ranch Hand	128	19 (14.8)	1.76 (0.81,3.83)	0.154
	Comparison	134	12 (9.0)		
Enlisted Groundcrew	Ranch Hand	321	27 (8.4)	0.97 (0.57,1.64)	0.901
	Comparison	426	39 (9.2)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1985 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1992 are provided for reference purposes for participants who attended the 1985 and 1997 examinations. Statistical analyses are based only on participants who had normal peripheral pulses in 1985 (see Chapter 7, Statistical Methods).

Table 14-38. Longitudinal Analysis of Peripheral Pulses (Continued)

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN			
	Number (%) Abnormal/(n) Examination		
Initial Dioxin	1985	1992	1997
Low	15 (10.1) (149)	9 (6.3) (144)	16 (10.7) (149)
Medium	20 (12.7) (158)	17 (11.0) (155)	22 (13.9) (158)
High	13 (8.4) (154)	9 (6.0) (149)	15 (9.7) (154)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1985			
Initial Dioxin	n in 1997	Number (%) Abnormal in 1997	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	134	14 (10.4)	1.11 (0.85,1.45)	0.434
Medium	138	17 (12.3)		
High	141	12 (8.5)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1992 are provided for reference purposes for participants who attended the 1985 and 1997 examinations. Statistical analyses are based only on participants who had normal peripheral pulses in 1985 (see Chapter 7, Statistical Methods).

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY			
	Number (%) Abnormal/(n) Examination		
Dioxin Category	1985	1992	1997
Comparison	113 (11.2) (1,013)	81 (8.2) (988)	111 (11.0) (1,013)
Background RH	49 (13.8) (355)	30 (8.7) (345)	40 (11.3) (355)
Low RH	22 (9.8) (224)	13 (6.0) (217)	30 (13.4) (224)
High RH	26 (11.0) (237)	22 (9.5) (231)	23 (9.7) (237)
Low plus High RH	48 (10.4) (461)	35 (7.8) (448)	53 (11.5) (461)

Table 14-38. Longitudinal Analysis of Peripheral Pulses (Continued)

Dioxin Category	Normal in 1985: n in 1997	Normal in 1985: Number (%) Abnormal in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	900	86 (9.6)		
Background RH	306	32 (10.5)	0.98 (0.63,1.52)	0.934
Low RH	202	25 (12.4)	1.23 (0.76,1.99)	0.408
High RH	211	18 (8.5)	1.22 (0.70,2.11)	0.482
Low plus High RH	413	43 (10.4)	1.22 (0.82,1.82)	0.325

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1992 are provided for reference purposes for participants who attended the 1985 and 1997 examinations. Statistical analyses are based only on participants who had normal peripheral pulses in 1985 (see Chapter 7, Statistical Methods).

14.3 DISCUSSION

Cardiovascular diseases are among the most common encountered by the primary care physician. In practice, the diagnosis of cardiovascular disease is based primarily on the noninvasive data analyzed in the current chapter. Specifically, the history, physical examination, chest x ray, and resting ECG remain highly reliable indices that can alert the clinician to the presence of underlying cardiovascular disease and indicate the need for additional, more specific, noninvasive or invasive studies. Although arbitrary, dividing data collection into central and peripheral cardiovascular functions is convenient and forms a reasonable basis for comparison of the cohorts under study.

The limitations of the history in cardiovascular diagnosis deserve emphasis. In peripheral vascular disease, for example, signs and symptoms will vary depending on the degree of development of collateral circulatory channels. While hemodynamically significant arterial disease of the lower extremities is usually associated with claudication, severe carotid occlusive disease can be present in the absence of symptoms of transient cerebral ischemia. Further, conclusive evidence shows that advanced coronary artery disease can occur in the absence of angina and be present as “silent” myocardial ischemia. Lastly, it is well recognized that the cardiovascular history, as related by patients, is often subject to error. The generic term “heart attack,” for example, can be used to describe any type of cardiac event from an isolated episode of unstable angina or arrhythmia to a myocardial infarction. These imperfections highlight the importance of the medical record verification conducted in this study.

In the cardiovascular assessment particularly, the physical examination can provide valuable clues to the presence of asymptomatic but significant underlying disease. Steps were taken to simplify data collection and reduce differences among the examining physicians. All blood pressure readings, for example, were taken by automated sphygmomanometric instruments. Auscultory endpoints—murmurs and bruits—were recorded as present or absent by anatomic location, thus eliminating speculation as to specific

valvular or vessel origin and hemodynamic significance. As markers of occult arterial occlusive disease, vascular bruits are relatively easy to detect and were carefully sought over the carotid, abdominal, and femoral vessels.

The data relevant to this chapter included the resting ECG, the standard two-view chest x ray (discussed in Chapter 18, Pulmonary Assessment) and Doppler arterial vascular studies. The test used can confirm diagnoses that can be made based on data available in the current assessment. For example, when correlated with the history and physical examination, the chest x ray and ECG enable the clinician to draw highly accurate conclusions regarding the presence and hemodynamic significance of valvular heart disease of any etiology. As defined by the chest x ray, the pulmonary vascularity can provide reliable clues to the presence of global left ventricular dysfunction with pulmonary venous congestion and of pulmonary hypertension of any cause.

In the analyses of verified historical variables, hypertension, myocardial infarction, transient ischemic attack, and stroke were similar in Ranch Hands and Comparisons. In the 1997 examinations, in contrast to 1992, Ranch Hands were more likely to have a history of heart disease (66.1% vs. 60.8%) across all occupational strata, particularly in the enlisted flyer category. In none of the physical examination or electrocardiographic variables were any significant group differences defined. The prevalence of funduscopic abnormalities, peripheral pulse deficits, and intermittent claudication, all more common in Ranch Hands than Comparisons in the 1992 examination, is now essentially the same in the two cohorts.

Serum dioxin analyses yielded several significant results. In the unadjusted analysis, a significant positive dose-response effect was noted in Ranch Hands in the association of hypertension with 1987 serum dioxin levels (34.0%, 38.0%, and 49.1% in the low, medium, and high categories, respectively), an association that remained significant after adjustment for covariates. Similarly, although the association was less significant, a positive dose-response effect was noted between the electrocardiographic evidence of a myocardial infarction and both initial and 1987 serum dioxin levels. Ranch Hands in the highest dioxin category were more likely than Comparisons to have tachycardia, as determined by the electrocardiograph. In contrast, although Ranch Hands were more likely than Comparisons to have a history of heart disease, a significant inverse dose-response effect was noted in relation to both extrapolated initial and 1987 serum dioxin levels. These results are consistent with those from both the 1987 and 1992 examinations.

With few exceptions, dependent variable-covariate analyses confirmed well-established associations. By a medical records review and by abnormalities detected on physical examinations, cardiovascular disease was associated significantly with the classic risk factors of age, cigarette use, and, particularly, diabetes. Obesity proved to be a significant risk factor for the development of heart disease and for numerous electrocardiographic abnormalities but not to the occurrence of myocardial infarction historically or by ECG. Alcohol consumption was associated strongly with the development of hypertension but did not have the protective effect on the occurrence of myocardial infarction that was noted in the 1992 examination. The increased prevalence of pulse deficits in association with alcohol consumption may have been mediated by concomitant cigarette use. Finally, consistent with the results of the 1987 and 1992 examinations, type A personality traits were not found to be associated with an increased risk for the development of cardiovascular disease.

In the longitudinal analysis, a comparable increase in the prevalence of peripheral pulse deficits was noted in both the Ranch Hand and Comparison cohorts between the 1992 and 1997 examinations. Although none of the group differences was statistically significant, Ranch Hands continued to have a slightly greater prevalence of pulse deficits than Comparisons at all sites examined. Two of the six analyses, the posterior tibial and femoral pulses, yielded evidence for a significant or marginally significant association

of pulse deficits with categorized dioxin. Consistent with all previous examinations, Comparisons were found to be at slightly greater risk than Ranch Hands for the development of systolic hypertension by discrete analysis, but group differences remain nonsignificant.

In contrast to prior examinations, the current study has documented that Ranch Hands are more likely than Comparisons to have historical evidence for heart disease (excluding essential hypertension) but are no longer at greater risk for the occurrence of pulse deficits. By all other indices, the prevalence of cardiovascular disease appears similar in both cohorts. For the first time, there is evidence that dioxin exposure may be a risk factor for the development of hypertension and myocardial infarction. As of 1997, the verified history of essential hypertension was associated with 1987 dioxin, and the evidence of prior myocardial infarction from the ECG was associated with initial dioxin.

14.4 SUMMARY

The cardiovascular assessment was based on a medical records review and verification, physical examination and ECG determinations, and an ICVI index based on participant responses to three questions regarding leg pain. Variables constructed from the medical records review included essential hypertension, heart disease (excluding essential hypertension), myocardial infarction, and stroke or transient ischemic attack. The physical examination findings, the ECG determinations, and the ICVI index investigated the central cardiac function and peripheral vascular function. Each health endpoint was examined for an association with exposure group (Model 1), initial dioxin (Model 2), categorized dioxin (Model 3), and 1987 dioxin levels (Model 4). Significant results from the adjusted analyses are presented below.

14.4.1 Model 1: Group Analysis

The adjusted group analysis revealed that Ranch Hands had a significantly higher percentage of participants with a history of heart disease (excluding essential hypertension) than did Comparisons when all occupational strata were combined. Stratifying by occupation revealed a significantly higher percentage of Ranch Hand enlisted flyers with a history of heart disease than Comparison enlisted flyers. Ranch Hand enlisted groundcrew had a significantly lower percentage of abnormal funduscopic examination results than Comparison enlisted groundcrew. Ranch Hand enlisted groundcrew also had a marginally significantly lower percentage of abnormal overall ECG findings than Comparison enlisted groundcrew. The results of all unadjusted and adjusted Model 1 analyses are summarized in Table 14-39.

Table 14-39. Summary of Group Analysis (Model 1) for Cardiovascular Variables (Ranch Hands vs. Comparisons)

	UNADJUSTED			
Variable	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Medical Records				
Essential Hypertension (D)	ns	ns	NS	ns
Heart Disease (Excluding Essential Hypertension) (D)	+0.013	NS	+0.003	NS
Myocardial Infarction (D)	NS	ns	NS	NS
Stroke or Transient Ischemic Attack (D)	NS	NS	ns	NS
Physical Examination				
Systolic Blood Pressure (C)	ns	ns	ns	ns
Systolic Blood Pressure (D)	ns	NS	NS	ns

Table 14-39. Summary of Group Analysis (Model 1) for Cardiovascular Variables (Ranch Hands vs. Comparisons) (Continued)

Variable	UNADJUSTED			
	All	**Officer**	**Enlisted Flyer**	**Enlisted Groundcrew**
Diastolic Blood Pressure (C)	ns	ns	NS	ns
Diastolic Blood Pressure (D)	NS	NS	NS	ns
Heart Sounds (D)	ns	ns	ns	ns
Overall Electrocardiograph (ECG) (D)	NS	NS	NS	ns*
ECG: Right Bundle Branch Block (D)	ns	ns	NS	ns
ECG: Left Bundle Branch Block (D)	ns	ns	NS	ns
ECG: Non-Specific ST- and T-Wave Changes (D)	NS	NS	NS	ns
ECG: Bradycardia (D)	ns	ns	NS	ns
ECG: Tachycardia (D)	NS	NS	NS	NS
ECG: Arrhythmia (D)	NS	NS	NS	ns
ECG: Evidence of Prior Myocardial Infarction (D)	ns	ns	ns	ns
ECG: Other Diagnoses (D)	NS	NS	--	NS
Funduscopic Examination (D)	ns	NS	NS	–0.033
Carotid Bruits (D)	NS	ns	NS	ns
Radial Pulses (D)	NS	NS	--	NS
Femoral Pulses (D)	NS*	NS	NS	NS
Popliteal Pulses (D)	NS	ns	NS	NS
Dorsalis Pedis Pulses (D)	NS	NS	NS	ns
Posterior Tibial Pulses (D)	NS	NS	NS	NS
Leg Pulses (D)	NS	NS	NS	ns
Peripheral Pulses (D)	NS	NS	NS	ns
Self-reported Questionnaire				
Intermittent Claudication and Vascular Insufficiency Index (ICVI) (D)	NS	NS	ns	NS

Note: NS or ns: Not significant (p>0.10).
NS* or ns*: Marginally significant (0.05<p≤0.10).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00.
–: Relative risk <1.00.
--: Analysis not performed because of the sparse number of participants with an abnormality.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes a relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 14-39. Summary of Group Analysis (Model 1) for Cardiovascular Variables (Ranch Hands vs. Comparisons) (Continued)

Variable	ADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Medical Records				
Essential Hypertension (D)	ns	ns	NS	ns
Heart Disease (Excluding Essential Hypertension) (D)	+0.018	NS	+0.004	NS
Myocardial Infarction (D)	NS	ns	NS	ns
Stroke or Transient Ischemic Attack (D)	NS	NS	--	NS
Physical Examination				
Systolic Blood Pressure (C)	ns	ns	NS	ns
Systolic Blood Pressure (D)	ns	ns	NS	ns
Diastolic Blood Pressure (C)	NS	ns	NS	NS
Diastolic Blood Pressure (D)	NS	NS	NS	ns
Heart Sounds (D)	ns	ns	ns	ns
Overall Electrocardiograph (ECG) (D)	ns	NS	NS	ns*
ECG: Right Bundle Branch Block (D)	ns	ns	NS	ns
ECG: Left Bundle Branch Block (D)	ns	ns	--	ns
ECG: Non-Specific ST- and T-Wave Changes (D)	NS	NS	NS	ns
ECG: Bradycardia (D)	ns	ns	NS	ns
ECG: Tachycardia (D)	NS	--	--	NS
ECG: Arrhythmia (D)	NS	NS	NS	ns
ECG: Evidence of Prior Myocardial Infarction (D)	ns	ns	NS	ns
ECG: Other Diagnoses (D)	NS	--	--	NS
Funduscopic Examination (D)	ns	NS	NS	–0.047
Carotid Bruits (D)	ns	ns	NS	ns
Radial Pulses (D)	NS	NS	--	NS
Femoral Pulses (D)	NS	NS	NS	NS
Popliteal Pulses (D)	NS	ns	ns	NS
Dorsalis Pedis Pulses (D)	ns	NS	NS	ns
Posterior Tibial Pulses (D)	NS	NS	NS	NS
Leg Pulses (D)	NS	NS	NS	ns
Peripheral Pulses (D)	NS	NS	NS	ns
Self-reported Questionnaire				
Intermittent Claudication and Vascular Insufficiency Index (ICVI) (D)	ns	NS	ns	NS

Note: NS or ns: Not significant ($p>0.10$).
ns*: Marginally significant ($0.05<p\leq0.10$).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00.
–: Relative risk <1.00.
--: Analysis not performed because of the sparse number of participants with an abnormality.

P-value given if $p\leq0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes a relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

14.4.2 Model 2: Initial Dioxin Analysis

Model 2 analyses revealed a significant positive association between initial dioxin and evidence of prior myocardial infarction from the ECG. The results of all unadjusted and adjusted Model 2 analyses are summarized in Table 14-40.

Table 14-40. Summary of Initial Dioxin Analysis (Model 2) for Cardiovascular Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Essential Hypertension (D)	NS	NS
Heart Disease (Excluding Essential Hypertension) (D)	−0.001	ns
Myocardial Infarction (D)	NS	NS
Stroke or Transient Ischemic Attack (D)	NS	NS
Physical Examination		
Systolic Blood Pressure (C)	ns	ns
Systolic Blood Pressure (D)	−0.031	ns
Diastolic Blood Pressure (C)	NS	NS
Diastolic Blood Pressure (D)	NS	NS
Heart Sounds (D)	NS	NS
Overall Electrocardiograph (ECG) (D)	ns	NS
ECG: Right Bundle Branch Block (D)	ns	NS
ECG: Left Bundle Branch Block (D)	ns	--
ECG: Non-Specific ST- and T-Wave Changes (D)	ns	NS
ECG: Bradycardia (D)	ns	ns
ECG: Tachycardia (D)	NS	--
ECG: Arrhythmia (D)	ns	NS
ECG: Evidence of Prior Myocardial Infarction (D)	NS	+0.012
ECG: Other Diagnoses (D)	NS	--
Funduscopic Examination (D)	ns	NS
Carotid Bruits (D)	NS	NS
Radial Pulses (D)	ns	--
Femoral Pulses (D)	ns	NS
Popliteal Pulses (D)	ns	ns
Dorsalis Pedis Pulses (D)	ns	NS
Posterior Tibial Pulses (D)	NS	NS
Leg Pulses (D)	ns	NS
Peripheral Pulses (D)	ns	NS
Self-reported Questionnaire		
Intermittent Claudication and Vascular Insufficiency Index (ICVI) (D)	ns	NS

Note: NS or ns: Not significant (p>0.10).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00.
−: Relative risk <1.00.
--: Analysis not performed because of the sparse number of Ranch Hands with an abnormality.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or slope nonnegative for continuous analysis. A lowercase "ns" denotes a relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

14.4.3 Model 3: Categorized Dioxin Analysis

The adjusted Model 3 analysis revealed a significantly higher occurrence of heart disease for Ranch Hands in the background dioxin category than for Comparisons. A significantly lower prevalence of abnormal heart sounds was found for Ranch Hands in the background dioxin category than for Comparisons. The percentage of Ranch Hands in the low dioxin category with a history of heart disease was marginally significantly greater than Comparisons. The prevalence of Ranch Hands in the low dioxin category with abnormal ECG findings was marginally significantly smaller than Comparisons. Ranch Hands in the high dioxin category had a significantly greater prevalence of tachycardia and other ECG diagnoses than Comparisons. The results of all unadjusted and adjusted Model 3 analyses are summarized in Table 14-41.

Table 14-41. Summary of Categorized Dioxin Analysis (Model 3) for Cardiovascular Variables (Ranch Hands vs. Comparisons)

	UNADJUSTED			
Variable	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Medical Records				
Essential Hypertension (D)	ns	ns	NS	NS
Heart Disease (Excluding Essential Hypertension) (D)	+0.005	+0.011	ns	NS
Myocardial Infarction (D)	ns	ns	NS	NS
Stroke or Transient Ischemic Attack (D)	NS	ns	NS	ns
Physical Examination				
Systolic Blood Pressure (C)	ns	NS	ns*	ns
Systolic Blood Pressure (D)	NS	NS	ns	ns
Diastolic Blood Pressure (C)	ns	ns	NS*	NS
Diastolic Blood Pressure (D)	ns	NS	NS	NS
Heart Sounds (D)	–0.047	ns	ns	ns
Overall Electrocardiograph (ECG) (D)	NS	ns	ns	ns
ECG: Right Bundle Branch Block (D)	ns	ns	NS	ns
ECG: Left Bundle Branch Block (D)	NS	ns	ns	ns
ECG: Non-Specific ST- and T-Wave Changes (D)	ns	NS	NS	NS
ECG: Bradycardia (D)	ns	ns	–0.042	–0.020
ECG: Tachycardia (D)	NS	ns	+0.033	NS
ECG: Arrhythmia (D)	ns	NS	ns	NS
ECG: Evidence of Prior Myocardial Infarction (D)	ns	NS	ns	ns
ECG: Other Diagnoses (D)	NS	ns	+0.042	NS
Funduscopic Examination (D)	ns	NS	ns	NS
Carotid Bruits (D)	ns	ns	NS	NS
Radial Pulses (D)	NS	NS	NS	NS
Femoral Pulses (D)	NS	NS	NS	NS*
Popliteal Pulses (D)	ns	NS	NS	NS
Dorsalis Pedis Pulses (D)	ns	NS	ns	NS
Posterior Tibial Pulses (D)	NS	NS	NS	NS
Leg Pulses (D)	ns	NS	NS	NS
Peripheral Pulses (D)	ns	NS	NS	NS

Table 14-41. Summary of Categorized Dioxin Analysis (Model 3) for Cardiovascular Variables (Ranch Hands vs. Comparisons) (Continued)

	UNADJUSTED			
Variable	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Self-reported Questionnaire				
Intermittent Claudication and Vascular Insufficiency Index (ICVI) (D)	ns	NS	NS	NS

Note: NS or ns: Not significant (p>0.10).
NS* or ns*: Marginally significant (0.05<p≤0.10).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00.
–: Relative risk <1.00.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes a relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

	ADJUSTED			
Variable	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Medical Records				
Essential Hypertension (D)	ns	ns	NS	NS
Heart Disease (Excluding Essential Hypertension) (D)	+0.032	NS*	NS	NS
Myocardial Infarction (D)	ns	ns	NS	NS
Stroke or Transient Ischemic Attack (D)	ns	ns	NS	NS
Physical Examination				
Systolic Blood Pressure (C)	NS	ns	ns	ns
Systolic Blood Pressure (D)	NS	NS	ns	ns
Diastolic Blood Pressure (C)	ns	ns	NS	NS
Diastolic Blood Pressure (D)	ns	ns	NS	NS
Heart Sounds (D)	–0.041	ns	NS	ns
Overall Electrocardiograph (ECG) (D)	NS	ns*	NS	ns
ECG: Right Bundle Branch Block (D)	NS	ns	NS	ns
ECG: Left Bundle Branch Block (D)	ns	ns	--	--
ECG: Non-Specific ST- and T-Wave Changes (D)	ns	ns	NS	NS
ECG: Bradycardia (D)	ns	ns	ns	ns*
ECG: Tachycardia (D)	NS	--	+0.032	--
ECG: Arrhythmia (D)	ns	NS	NS	NS
ECG: Evidence of Prior Myocardial Infarction (D)	ns	ns	NS	ns
ECG: Other Diagnoses (D)	NS	--	+0.050	--
Funduscopic Examination (D)	NS	ns	ns	ns
Carotid Bruits (D)	NS	ns	NS	ns
Radial Pulses (D)	NS	NS	NS	NS
Femoral Pulses (D)	NS	NS	NS	NS

Table 14-41. Summary of Categorized Dioxin Analysis (Model 3) for Cardiovascular Variables (Ranch Hands vs. Comparisons) (Continued)

	ADJUSTED			
Variable	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Popliteal Pulses (D)	ns	NS	NS	NS
Dorsalis Pedis Pulses (D)	ns	ns	ns	ns
Posterior Tibial Pulses (D)	NS	NS	NS	NS
Leg Pulses (D)	NS	NS	ns	ns
Peripheral Pulses (D)	NS	NS	ns	NS
Self-reported Questionnaire				
Intermittent Claudication and Vascular Insufficiency Index (ICVI) (D)	ns	ns	NS	NS

Note: NS or ns: Not significant ($p>0.10$).
NS* or ns*: Marginally significant ($0.05<p\leq 0.10$).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00.
–: Relative risk <1.00.
--: Analysis not performed because of the sparse number of participants with an abnormality.

P-value given if $p\leq 0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes a relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

14.4.4 Model 4: 1987 Dioxin Level Analysis

The adjusted Model 4 analysis revealed a significant positive association between essential hypertension and 1987 dioxin. A marginally significant association between the evidence of a prior myocardial infarction, as determined from the ECG, and 1987 dioxin also was observed. The results of all unadjusted and adjusted Model 4 analyses are summarized in Table 14-42.

Table 14-42. Summary of 1987 Dioxin Analysis (Model 4) for Cardiovascular Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Essential Hypertension (D)	+<0.001	+0.011
Heart Disease (Excluding Essential Hypertension) (D)	–0.004	ns
Myocardial Infarction (D)	NS	NS
Stroke or Transient Ischemic Attack (D)	ns	NS
Physical Examination		
Systolic Blood Pressure (C)	NS	ns
Systolic Blood Pressure (D)	NS	ns*
Diastolic Blood Pressure (C)	+0.014	NS
Diastolic Blood Pressure (D)	NS	NS

Table 14-42. Summary of 1987 Dioxin Analysis (Model 4) for Cardiovascular Variables (Ranch Hands Only) (Continued)

Variable	Unadjusted	Adjusted
Heart Sounds (D)	NS	NS
Overall Electrocardiograph (ECG) (D)	ns	NS
ECG: Right Bundle Branch Block (D)	NS	NS
ECG: Left Bundle Branch Block (D)	ns	ns
ECG: Non-Specific ST- and T-Wave Changes (D)	NS	NS
ECG: Bradycardia (D)	ns*	ns
ECG: Tachycardia (D)	NS	NS
ECG: Arrhythmia (D)	ns	NS
ECG: Evidence of Prior Myocardial Infarction (D)	NS	NS*
ECG: Other Diagnoses (D)	NS	NS
Funduscopic Examination (D)	NS	NS
Carotid Bruits (D)	NS	ns
Radial Pulses (D)	ns	ns
Femoral Pulses (D)	NS	NS
Popliteal Pulses (D)	ns	NS
Dorsalis Pedis Pulses (D)	ns	NS
Posterior Tibial Pulses (D)	NS	NS
Leg Pulses (D)	NS	NS
Peripheral Pulses (D)	NS	NS
Self-reported Questionnaire		
Intermittent Claudication and Vascular Insufficiency Index (ICVI) (D)	NS	NS

Note: NS or ns: Not significant (p>0.10).
NS* or ns*: Marginally significant (0.05<p≤0.10).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00 for discrete analysis; slope nonnegative for continuous analysis.
–: Relative risk <1.00.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or slope nonnegative for continuous analysis. A lowercase "ns" denotes a relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

14.5 CONCLUSION

Analyses revealed that Ranch Hands had a significantly higher percentage of participants with a history of heart disease (excluding essential hypertension) than did Comparisons and, in particular, within enlisted flyers. However, the risk of disease was not significantly increased in Ranch Hand enlisted groundcrew—the military occupation with the highest dioxin levels. The association between heart disease and initial dioxin for Ranch Hands showed a negative dose-response trend, with heart disease decreasing as initial dioxin increased. Furthermore, Ranch Hands in the background and the low dioxin categories had more heart disease than did Comparisons, but this increase was not seen in Ranch Hands in the high dioxin category. Increases in tachycardia and other ECG findings, such as pre-excitation, were seen for Ranch Hands in the high dioxin category, although the analyses were based on a sparse number of abnormalities. A significant positive association between initial dioxin and evidence of prior myocardial infarction from the ECG was observed in Ranch Hands, and a marginally significant positive

association was observed between 1987 dioxin and evidence of prior myocardial infarction from the ECG. A positive association between 1987 dioxin and essential hypertension also was observed in Ranch Hands. In contrast to previous AFHS examinations, no relation was found between peripheral pulses and any measures of exposure.

In summary, in contrast to prior examinations, the current study has documented that Ranch Hands are more likely than Comparisons to have historical evidence for heart disease (excluding essential hypertension) but are no longer at greater risk for the occurrence of pulse deficits. By all other indices, the prevalence of cardiovascular disease appears similar in both cohorts. For the first time, there is evidence that levels of dioxin may be a risk factor for the development of essential hypertension and prior myocardial infarction as indicated by interpretation of the ECG. As of 1997, the verified history of essential hypertension was associated with 1987 dioxin, and the evidence of prior myocardial infarction from the ECG was associated with initial dioxin. These findings, in conjunction with the increase in the number of deaths caused by diseases of the circulatory system for Ranch Hand nonflying enlisted personnel based on the 1994 AFHS mortality update (34), showed associations with dioxin that require further observation. A biological mechanism for the relation between dioxin and heart disease is unknown at this time.

REFERENCES

1. Hermansky, S. J., T. L. Holcslaw, W. J. Murray, R. S. Markin, and S. J. Stohs. 1988. Biochemical and functional effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin on the heart of female rats. *Toxicology and Applied Pharmacology* 95:175-84.

2. Canga, L., R. Levi, and A. B. Rifkind. 1988. Heart as a target organ in 2,3,7,8-tetrachlorodibenzo-p-dioxin toxicity: Decreased beta-adrenergic responsiveness and evidence of increased intracellular calcium. *Proceedings of the National Academy of Sciences* 85:905-9.

3. Kelling, C. K., L. A. Menahan, and R. E. Peterson. 1987. Effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin treatment on mechanical function of the rat heart. *Toxicology and Applied Pharmacology* 91:497-501.

4. Brewster, D. W., F. Matsumura, and T. Akera. 1987. Effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin on guinea pig heart muscle. *Toxicology and Applied Pharmacology* 89:408-17.

5. Brewster, D. W., D. W. Bommbick, and F. Matsumura. 1988. Rabbit serum hypertriglyceridemia after administration of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Journal of Toxicology and Environmental Health* 25:495-507.

6. Brewster, D. W., and F. Matsumura. 1989. Differential effect of 2,3,7,8-tetrachlorodibenzo-p-dioxin on adipose tissue lipoprotein lipase activity in the guinea pig, rat, hamster, rabbit, and mink. *Comparative Biochemistry and Physiology* 93C:49-53.

7. Kociba, R. J., D. G. Keyes, J. E. Beyer, R. M. Carreon, C. E. Wade, D. A. Dittenber, R. P. Kalnins, L. E. Frauson, C. N. Park, S. D. Barnard, R. A. Hummel, and C. G. Humiston. 1978. Results of a two-year chronic toxicity and oncogenicity study of 2,3,7,8-tetrachlorodibenzo-p-dioxin in rats. *Toxicology and Applied Pharmacology* 46:279-303.

8. Cantrell, S. M., L. H. Lutz, D. E. Tillitt, and M. Hannink. 1996. Embryotoxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD): The embryonic vasculature is a physiological target to TCDD-induced DNA damage and apoptotic cell death in Medaka (Orizias latipes). *Toxicology and Applied Pharmacology* 141:23.

9. Guiney, P. D., R. M. Smolowitz, R. E. Peterson, and J. J. Stegeman. 1997. Correlation of 2,3,7,8-tetrachlorodibenzo-p-dioxin induction of cytochrome P4501A in vascular endothelium with toxicity in early life stages of lake trout. *Toxicology and Applied Pharmacology* 143:256.

10. Schiller, C. M., C. M. Adcock, and R. A. Moore. 1985. Effect of 2,3,7,8-tetrachlorodibenzo-p-dioxin and fasting on body weight and lipid parameters in rats. *Toxicology and Applied Pharmacology* 81:356-61.

11. Jovanovich, L., S. Levin, and M. Kahn. 1987. Significance of mirex-caused hypoglycemia and hyperlipidemia in rats. *Journal of Biochemistry and Toxicology* 2:203-13.

12. Swift, L. L., T. A. Gasiewicz, and G. D. Dunn. 1981. Characterization of the hyperlipidemia in guinea pigs induced by 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Toxicology and Applied Pharmacology* 59:489-99.

13. Moses, M., R. Lilis, K. D. Crow, J. Thornton, A. Fischbein, H. A. Anderson, and I. J. Selikoff. 1984. Health status of workers with past exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin in the manufacture of 2,4,5-trichlorophenoxyacetic acid: Comparison of findings with and without chloracne. *American Journal of Industrial Medicine* 5:161-82.

14. Suskind, R. R., and V. S. Hertzberg. 1984. Human health effects of 2,4,5-T and its toxic contaminants. *Journal of the American Medical Association* 251:2372-80.

15. Zack, J. A., and W. R. Gaffey. 1983. A mortality study of workers employed at the Monsanto company plant in Nitro, West Virginia. *Environmental Science Research* 26:575-91.

16. Bond, G. G., M. G. Ott, F. E. Brenner, and R. R. Cook. 1983. Medical and morbidity surveillance findings among employees potentially exposed to TCDD. *British Journal of Industrial Medicine* 40:318-24.

17. Von Benner, A., L. Edler, K. Mayer, and A. Zober. 1994. 'Dioxin' investigation program of the chemical industry professional association. *Arbeitsmedizin Sozialmedizin Praventivmedizin* 29:11-6.

18. Bertazzi, P. A., C. Zocchetti, A. C. Pesatori, S. Guercilena, M. Sanarico, and L. Radice. 1989. Mortality in an area contaminated by TCDD following an industrial incident. *Medicina del Lavoro* (Italy) 80:316-29.

19. Bertazzi, P. A., C. Zocchetti, A. C. Pesatori, S. Guercilena, M. Sanarico, and L. Radice. 1989. Ten-year mortality study of the population involved in the Seveso incident in 1976. *American Journal of Epidemiology* 129:1187-200.

20. Zack, J. A., and R. R. Suskind. 1980. The mortality experience of workers exposed to tetrachlorodibenzodioxin in a trichlorophenol process accident. *Journal of Occupational Medicine* 22:11-4.

21. Zober, A., M. G. Ott, and P. Messerer. 1994. Morbidity follow-up study of BASF employees exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) after a 1953 chemical reactor incident. *Occupational and Environmental Medicine* 51:469-86.

22. Ott, M. G., A. Zober, and C. Germann. 1994. Laboratory results for selected target organs in 138 individuals occupationally exposed to TCDD. *Chemosphere* 29:2423-37.

23. Kogan, M. D., and R. W. Clapp. 1985. Mortality among Vietnam veterans in Massachusetts, 1972-1983. Massachusetts Office of the Commissioner of Veterans Services, Agent Orange Program.

24. Fett, M. J., J. R. Nairn, D. M. Cobbin, and M. A. Adena. 1987. Mortality among Australian conscripts of the Vietnam conflict era. II. Causes of death. *American Journal of Epidemiology* 125:878-84.

25. Anderson, H. A., L. P. Hanrahan, M. Jensen, D. Laurin, W.-Y. Yick, and P. Wiegman. 1986. Wisconsin Vietnam veteran mortality study: proportionate mortality ratio study results. Madison: Wisconsin Division of Health.

26. Centers for Disease Control (CDC). 1987. Postservice mortality among Vietnam veterans. *Journal of the American Medical Association* 257:790-5.

27. Centers for Disease Control. 1988. Health status of Vietnam veterans. II. Physical health. *Journal of the American Medical Association* 259:2708-14.

28. Pollei, S., F. A. Mettler Jr., C. A. Kelsey, M. R. Walters, and R. E. White. 1986. Follow-up chest radiographs in Vietnam veterans: Are they useful? *Radiology* 161:101-2.

29. Watanabe, K. K., H. K. Kang, and T. L. Thomas. 1991. Mortality among Vietnam veterans: with methodological considerations. *Journal of Occupational Medicine* 33:780-5.

30. Thomas, T. L., and H. K. Kang. 1990. Mortality and morbidity among Army Chemical Corps Vietnam veterans: a preliminary report. *American Journal of Industrial Medicine* 18:665-73.

31. Thomas, T. L., H. Kang, and N. Dalager. 1991. Mortality among women Vietnam veterans, 1973-1987. *American Journal of Epidemiology* 134:973-80.

32. Eisen, S., J. Goldberg, W. R. True, and W. G. Henderson. 1991. A co-twin control study of the effects of the Vietnam war on the self-reported physical health of veterans. *American Journal of Epidemiology* 134:49-59.

33. Stellman, S. D., J. M. Stellman, and J. F. Sommer, Jr. 1988. Health and reproductive outcomes among American Legionnaires in relation to combat and herbicide exposure in Vietnam. *Environmental Research* 47:150-74.

34. Roegner, R. H., W. D. Grubbs, M. B. Lustik, A. S. Brockman, S. C. Henderson, D. E. Williams, W. H. Wolfe, J. E. Michalek, and J. C. Miner. 1991. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides. Serum dioxin analysis of 1987 examination results. NTIS: AD A 237 516-24. United States Air Force School of Aerospace Medicine, Brooks Air Force Base, Texas.

35. Grubbs, W. D., W. H. Wolfe, J. E. Michalek, D. E. Williams, M. B. Lustik, A. S. Brockman, S. C. Henderson, F. R. Burnett, R. G. Land, D. J. Osborne, V. K. Rocconi, M. E. Schreiber, J. C. Miner, G. L. Henriksen, and J. A. Swaby. 1995. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final Report. 1992 Followup Examination Results. NTIS: AD A 304 306, 304 308-316. United States Air Force School of Aerospace Medicine, Brooks Air Force Base, Texas.

36. Wolfe, W. H., J. E. Michalek, and J. C. Miner. 1994. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Mortality update - 1994. Epidemiologic Research Division, Armstrong Laboratory, Human Systems Center, Brooks Air Force Base, Texas.

37. Flesch-Janys, D., J. Berger, P. Gurn, A. Manz, S. Nagel, H. Waltsgott, and J. H. Dwyer. 1995. Exposure to polychlorinated dioxins and furans (PCDD/F) and mortality in a cohort of workers from a herbicide-producing plant in Hamburg, Federal Republic of Germany. *American Journal of Epidemiology* 142(11):1165-75.

38. Henriksen, G. L., N. S. Ketchum, J. E. Michalek, and J. A. Swaby. 1997. Serum dioxin and diabetes mellitus in veterans of Operation Ranch Hand. *Epidemiology* 8:252-8.

39. Assennato, G., D. Cervino, E. A. Emmett, G. Longo, and F. Merlo. 1989. Follow-up of subjects who developed chloracne following TCDD exposure at Seveso. *American Journal of Industrial Medicine* 16:119-25.

40. Fingerhut, M. A., W. E. Halperin, D. A. Marlow, L. A. Piacitelli, P. A. Honchar, M. H. Sweeney, A. L. Greife, P. A. Dill, K. Steenland, and A. J. Suruda. 1991. Cancer mortality in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *New England Journal of Medicine* 324(4):212-8.

41. Martin, J. V. 1984. Lipid abnormalities in workers exposed to dioxin. *British Journal of Industrial Medicine* 41:254-6.

42. Ashe, W. F., and R. R. Siskind. 1982. Progress report - patients from Monsanto Chemical company, Nitro, West Virginia, 1959. Quoted by Hay, AWM in: *The chemical scythe: lessons of 2,4,5-T and dioxin.* New York and London: Plenum Press.

43. Oliver, R. M. 1975. Toxic effects of 2,3,7,8-tetrachlorodibenzo 1,4-dioxin on laboratory workers. *British Journal of Industrial Medicine* 32:49-53.

44. Walker, A. E., and J. V. Martin. 1979. Lipid profiles in dioxin exposed workers. *Lancet* i:446-7.

45. Lathrop, G. D., W. H. Wolfe, R. A. Albanese, and P. M. Moynahan. 1984. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Baseline Morbidity Study Results. NTIS: AD A-138-340. United States Air Force School of Aerospace Medicine, Brooks Air Force Base, Texas.

46. Wolfe, W. H., J. E. Michalek, J. C. Miner, A. Rahe, J. Silva, W. F. Thomas, W. D. Grubbs, M. B. Lustik, T. G. Karrison, R. H. Roegner, and D. E. Williams. 1990. Health status of Air Force veterans occupationally exposed to herbicides in Vietnam. I. Physical health. *Journal of the American Medical Association* 264:1824-31.

47. Hoffman, R. E., P. A. Stehr-Green, K. B. Webb, G. Evans, A. P. Knutsen, W. F. Schramm, J. L. Staake, B. B. Gibson, and K. K. Steinberg. 1986. Health effects of long-term exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Journal of the American Medical Association* 255:2031-38.

48. Stehr, P. A., G. Stein, H. Falk, E. Sampson, S. J. Smith, K. Steinberg, K. Webb, S. Ayres, and W. Schramm. 1986. A pilot epidemiologic study of possible health effects associated with 2,3,7,8-tetrachlorodibenzo-p-dioxin contamination in Missouri. *Archives of Environmental Health* 41:16-22.

49. Lathrop, G. D., S. G. Machado, T. G. Karrison, W. D. Grubbs, W. F. Thomas, W. H. Wolfe, J. E. Michalek, J. C. Miner, and M. R. Peterson. 1987. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: First followup examination results. NTIS: AD A 188262. United States Air Force School of Aerospace Medicine. Brooks Air Force Base, Texas.

50. Knapik, J. J., A. R. L. Burse, and J. A. Vogel. 1983. Height, weight, percent body fat, and indices of adiposity for young men and women entering the Army. *Aviation, Space, and Environmental Medicine* 54:223-31.

51. Jenkins, C. D., R. H. Roseman, and S. J. Zyzanski. 1974. Prediction of clinical coronary heart disease by a test for the coronary-prone behavior pattern. *New England Journal of Medicine* 290(23):1271-5.

52. Michalek, J. E., J. L. Pirkle, S. P. Caudill, R. C. Tripathi, D. G. Patterson Jr., and L. L. Needham. 1996. Pharmacokinetics of TCDD in Veterans of Operation Ranch Hand: 10-year Followup. *Journal of Toxicology and Environmental Health* 47:209-20.

53. Mausner, J. S., and A. K. Bahn. 1974. *Epidemiology – An Introductory Text.* Philadelphia: W. B. Saunders Company.

Table of Contents

List of Tables

15 HEMATOLOGIC ASSESSMENT

15.1 INTRODUCTION

15.1.1 Background

Experiments in laboratory animals have demonstrated that 2,3,7,8-tetrachlorodibenzo-p-dioxin (dioxin) is directly toxic to the hematopoietic system in several species. In one study, dioxin administered in low doses (0.70 μg/kg or 350 μg/kg of dioxin by oral gavage) to monkeys resulted in elevated neutrophil counts while higher doses were associated with lympho- and thrombocytopenia (1). A decrease in overall cellularity and an increase in the myeloid-erythroid ratio were noted in approximately half of the sternal bone marrow samples examined at the conclusion of the experiment.

Other animal studies have shown that the toxic effects of dioxin on the hematopoietic system vary depending on the dose employed and the species examined. In many reports, it is difficult to distinguish primary effects from those occurring secondary to systemic toxicity. One study in rats using gavage doses of dioxin varying from 0.001 to 1.0 μg/kg noted depressed red blood cell (RBC) counts and packed cell volumes in the high-dose group (2). In another rat experiment employing 10 μg/kg of dioxin orally, elevated erythrocyte, reticulocyte, and neutrophil counts were noted with reduction in mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), platelet counts, and clot retraction times—effects that the authors felt could be attributed to systemic toxicity with terminal dehydration (3). In a multispecies study, mice and guinea pigs given oral doses of dioxin varying from 0.1 μg/kg to 50 μg/kg were found to have dose-dependent reductions in leukocytes with relative lymphocytopenia within 1 week of dioxin administration, and thrombocytopenia and hemoconcentration were found in rats (4).

Several animal experiments, although designed primarily to investigate immunologic sequelae of dioxin exposure, have focused on selected hematologic elements, particularly macrophages and polymorphonuclear leukocytes, but whether the responses observed were secondary to inflammation or specific to dioxin is not known (3, 5–7).

More recent animal research relevant to the hematopoietic system has focused on the altered cellular differentiation associated with dioxin toxicity. In mice, progenitor cells were suppressed following exposure to dioxin in doses as low as 1.0 μg/kg of body weight, and in vitro studies demonstrated that myelotoxicity occurs by a direct inhibition of proliferating stem cells (8). A subsequent study from the same laboratory demonstrated a direct effect of dioxin on cultured lymphocytes resulting in a selective inhibition of B-cell differentiation into antibody-secretive cells (9). In these and other studies (10), the authors cite evidence for the role of the aryl hydrocarbon (Ah) receptor in mediating these myelo- and lymphotoxic effects. In another report, the presence of the Ah receptor was defined in the spleens of numerous primate species (11). Although Ah receptors have been isolated in the tissue of several human organs (12–17), the relevance of these observations to dioxin hematopoietic toxicity remains to be proven (18).

In general, human observational studies have shown fewer and less consistent hematologic findings than the structured animal experiments. Mortality and morbidity studies that have included hematologic data as endpoints have been based on populations exposed to dioxin by occupation (19–21), environmental contamination (22–26), consequent to industrial chemical accidents (27–33), and during military service in Southeast Asia (SEA) (34–39).

In the cancer mortality study reported by the National Institute of Occupational Safety and Health, one of few to incorporate serum dioxin data into the analyses, there was no significant increase in the relative risk of hematologic malignancies associated with exposure to dioxin in either the entire cohort or in a subcohort with more than 20 years of latency (19). Numerous studies have been conducted on cohorts that were exposed to dioxin by contamination of soil at the Quail Run (22–24) and Times Beach (25) residential areas of Missouri. With one exception, no differences were found in any of the hematologic parameters examined. In the Times Beach study, a statistically significant increase in the mean platelet count was noted in the exposed cohort relative to the unexposed, but the difference (281,927 mm^3 vs. 249,061 mm^3) was not considered clinically meaningful. A follow-up study, the first to report clinical hematologic indices in relation to tissue levels of dioxin (26), found no abnormalities in the complete blood count related to the body burden of dioxin.

A clinical epidemiological study was conducted 30 years after an explosion in a trichlorophenol plant in Nitro, West Virginia. The study compared 204 highly exposed employees, 86 percent of whom had developed chloracne, with 163 employees who were not exposed (27). No significant differences were found in the standard hematologic indices. A recent mortality experience study of 754 workers employed at the same plant, 122 of whom had sufficiently severe dioxin exposure to cause chloracne, found no increased mortality associated with all lymphatic and hematopoietic malignancies (32).

The monitoring of the populations heavily exposed to dioxin during the Seveso, Italy, hexachlorophene manufacturing plant explosion in 1976 and at the BASF chemical plant in 1953 continues to generate reports of medical surveillance. Although transient depression of the peripheral white blood cell (WBC) count after dioxin exposure has been documented (20, 21), a morbidity study of workers involved in the cleanup of the Seveso environs found no differences in selected hematologic indices (hemoglobin, WBC count, and platelets) between exposed subjects and controls (33). In the most recent report on the BASF population, exposed subjects had a significantly higher erythrocyte sedimentation rate than referents (6.53 mm/hr vs. 4.95 mm/hr), but no differences were noted in the WBC count, platelet count, or hemoglobin (20).

In previous reports of the Air Force Health Study (AFHS) (35–37), Ranch Hand participants were found to have slightly higher mean platelet counts than Comparisons and, in the 1987 follow-up examinations (37), a significantly greater percentage of abnormally high platelet counts as well. In the serum dioxin analysis of the 1987 examinations (38), Ranch Hands with the highest current serum dioxin levels had higher mean platelet and total WBC counts than Comparisons, results that raised the possibility of a chronic inflammatory response associated with dioxin levels. In the 1992 examinations, when the results were adjusted for covariates, no significant group differences were noted between the Ranch Hand and Comparison cohorts, nor was there any evidence for a persistent inflammatory response related to prior exposure to dioxin (39).

15.1.2 Summary of Previous Analyses of the Air Force Health Study

15.1.2.1 1982 Baseline Study Summary Results

The functional integrity of the hematopoietic system was assessed at the 1982 baseline examination by the measurement of eight peripheral blood variables: RBC count, WBC count, hemoglobin, hematocrit, MCV, MCH, mean corpuscular hemoglobin concentration (MCHC), and platelet count. These variables were analyzed in the discrete form to detect differences in the percentages of values outside the designed laboratory range, as well as analyzed in the continuous form to detect shifts in mean values between the Ranch Hand and Comparison groups.

The Ranch Hand group had a significantly higher adjusted mean MCV and MCH than the Comparison group (p=0.05 and p=0.04, respectively), although the magnitude of the difference was small in each case. The Ranch Hand adjusted mean values for five other parameters (i.e., RBC, WBC, hemoglobin, hematocrit, and MCHC) were nearly identical to the adjusted mean values of the Comparison group. The mean platelet count for Ranch Hands was marginally significantly greater than the Comparison mean count (p=0.06). The percent of abnormal values for these eight variables, as established by the upper and lower limits of normal, did not differ significantly between the two groups.

15.1.2.2 1985 Follow-up Study Summary Results

The same eight peripheral blood variables (i.e., RBC, WBC, hemoglobin, hematocrit, MCV, MCH, MCHC, and platelet count) were analyzed in the 1985 follow-up study. The unadjusted discrete analysis of the percent abnormal values, both low and high, showed no statistically significant difference between the Ranch Hand and Comparison groups for any of the hematologic variables. Similarly, in the adjusted discrete analyses, none of the adjusted relative risks was significant.

As no subgroup demonstrated consistent patterns of hematologic impairment, biologic relevance was not assigned to the interactions. The significant group differences found for MCV and MCH at the baseline examination were not present in the 1985 follow-up analyses. The covariate effects of age, race, occupation, and lifetime smoking history were highly significant for many of the hematologic variables.

The longitudinal analyses of MCV, MCH, and platelet count found a significant group difference for platelet count, with the Ranch Hands having an average decrease in platelet count between examinations and the Comparisons having an average increase. As a result, the baseline group difference (nonsignificant) in mean values approached equality at the 1985 follow-up examination.

In conclusion, none of the eight hematologic variable means was found to differ significantly between the Ranch Hand and Comparison groups. The expected effects of age, race, and smoking were demonstrated with most of the hematologic variables. The longitudinal analyses also suggested that neither group manifested an impairment of the hematopoietic system. Exposure index analyses did not support a plausible dose-response relation for any of the hematologic variables.

15.1.2.3 1987 Follow-up Study Summary Results

The hematologic status of the Ranch Hand and Comparison groups was assessed by the examination of the same eight variables used in the two previous examinations: RBC, WBC, hemoglobin, hematocrit, MCV, MCH, MCHC, and platelet count. There were no statistically significant differences between the Ranch Hand and Comparison groups for mean RBC count, hemoglobin, hematocrit, MCV, MCH, and MCHC, in analyses either unadjusted or adjusted for the covariates of age, race, occupation, current cigarette smoking, and lifetime cigarette smoking history. For WBC count, the unadjusted mean level was significantly greater in Ranch Hands than in Comparisons. The difference was not statistically significant after adjustment for covariates, nor were significant differences detected in the percentage of individuals with abnormal values.

Mean platelet counts also were significantly greater in Ranch Hands than in Comparisons, as was the percentage of individuals with abnormally high platelet counts. Longitudinal analyses detected a significantly greater decrease in the mean platelet count in Ranch Hands than in Comparisons, despite the higher overall mean count, from the baseline examination to the 1987 follow-up examination.

15.1.2.4 Serum Dioxin Analysis of 1987 Follow-up Study Summary Results

The number of dependent hematologic variables was increased from eight to nine with the addition of prothrombin time. Several of the nine variables showed an association with initial dioxin in the unadjusted model, but when the model was adjusted for covariates, the associations became nonsignificant. Hemoglobin and hematocrit were positively associated with current dioxin when time since duty in SEA was no more than 18.6 years and negatively associated with current dioxin when time since duty in SEA was greater than 18.6 years. For the discrete RBC count analysis, the relative risk of an abnormally low count was less than one when time since duty in SEA did not exceed 18.6 years and was greater than one when time since duty in SEA was more than 18.6 years. Because a low RBC count was considered abnormal for the purpose of these statistical analyses, the trend in relation to current dioxin was similar to that in the continuous analyses of hemoglobin and hematocrit. In the discrete analysis of prothrombin time, the trend in relation to current dioxin also was similar to that in the continuous analyses of hemoglobin and hematocrit. In the categorized current dioxin analyses, whenever the overall contrast showed significant, or marginally significant, differences among the categories, the mean level or percent abnormal in the three categories of Ranch Hands (i.e., officers, enlisted flyers, and enlisted groundcrew) tended to exceed the corresponding mean level or percent abnormal in the background category that consisted of Comparisons. The longitudinal analyses of MCV, MCH, and platelet count displayed no significant associations with dioxin.

In summary, the results of the previous analysis revealed no meaningful association between hematopoietic toxicity and dioxin exposure. Statistical analyses of two variables (WBC and platelet count) raised the possibility of subtle biologic effects that cannot be considered clinically meaningful but did point to the need for follow-up in future AFHS examinations. The increased platelet and WBC counts, in addition to the elevation of erythrocyte sedimentation rates (in the general health assessment), were thought to indicate the presence of a chronic inflammatory response to dioxin exposure.

15.1.2.5 1992 Follow-up Study Summary Results

The number of dependent hematologic variables was increased from 9 to 13 with elimination of MCV, MCH, and MCHC and the addition of RBC morphology (normal, abnormal), absolute neutrophils (segs), absolute neutrophils (bands), absolute lymphocytes, absolute monocytes, absolute eosinophils, and absolute basophils. The 13 endpoints analyzed in the hematology assessment provided a comprehensive evaluation of the three peripheral blood lines (erythrocytes, leukocytes, and platelets) and their relation to dioxin exposure. In the analyses of these variables, only platelet count exhibited significant associations with the herbicide exposure indices. Ranch Hands in the enlisted flyer and enlisted groundcrew categories possessed statistically significant higher mean platelet counts than Comparisons, although the result was not considered meaningful from a clinical point of view. Analyses using extrapolated levels of initial dioxin showed that Ranch Hands with high dioxin levels had significantly greater mean platelet count measurements than Comparisons. Platelet counts also were positively associated with current serum dioxin measurements, although the association became nonsignificant when adjusted for covariates. The 1992 follow-up results supported the results found in both the 1987 follow-up study and in the serum dioxin analysis of the 1987 follow-up study, but the biologic meaning was uncertain. Results from the 1987 follow-up study generated questions regarding the possibility of a subclinical inflammatory response associated with prior dioxin exposure. This was due to elevated mean WBC counts, platelet counts, and erythrocyte sedimentation rates in Ranch Hands. The 1992 follow-up study did not produce significant results to support this possibility. Therefore, in conclusion, there was no evidence from the 1992 follow-up study that suggested an association between hematopoietic toxicity and prior dioxin exposure.

15.1.3 Parameters for the 1997 Hematologic Assessment

15.1.3.1 Dependent Variables

The analysis of the hematologic assessment consisted of data from the laboratory examination only. No questionnaire or physical examination data were analyzed.

15.1.3.1.1 Laboratory Examination Data

A total of 13 hematology variables measured at the laboratory as part of the 1997 follow-up examination were analyzed statistically. These variables were the same as those studied in 1992 and included five cell counts, one RBC morphology, six measures of absolute blood counts, and a coagulation measure (prothrombin time). These variables were determined by routine hematologic procedures. In particular, the cell count indices were performed on the Coulter STKS® automated instrument, and prothrombin time was measured on the AMAX CS-190® instrument. All dependent variables were analyzed in the continuous form, except for the RBC morphology. RBC count, WBC count, hemoglobin, hematocrit, platelet count, prothrombin time, and the RBC morphology also were analyzed in their discrete form, using Scripps Clinic normal ranges as cutpoints. RBC count, WBC count, hemoglobin, hematocrit, and platelet count were trichotomized as abnormal low, normal, and abnormal high.

RBC morphology was constructed from a number of laboratory conditions, many of which were minor abnormalities. Conditions considered to be abnormal for the 1997 follow-up included rouleaux, Burr cells, moderate microcytes, many microcytes, moderate macrocytes, moderate amount of ovalocytes, hypochromia, anisocytosis, slight polychromasia, slight baso-stippling, moderate stomatocytes, schistocytes, Howell-Jolly bodies, few teardrop cells, and Papperheimer bodies. Participants with few ovalocytes, few microcytes, few macrocytes, and slight macrocytes were considered to be normal for RBC morphology.

Participants testing positive for the human immunodeficiency virus (HIV) were excluded from the analysis of all variables. Participants with a fever (body temperature greater than or equal to 100° Fahrenheit) at the time of the examination were excluded from the analysis of all variables except prothrombin time. Participants taking an anticoagulant (such as Coumadin®) or aspirin at the time of the examination also were excluded from the analysis of prothrombin time. In addition, one participant had a hemolyzed specimen for prothrombin time and was excluded from the analysis of this variable.

15.1.3.2 Covariates

Age, race, military occupation, current level of cigarette smoking (cigarettes/day), and lifetime cigarette smoking history (pack-years) were used as covariates in adjusted statistical analyses evaluating the hematologic dependent variables.

Age, race, and military occupation were determined from military records. Current cigarette smoking and lifetime cigarette smoking history were based on questionnaire data. For lifetime cigarette smoking history, the respondent's average smoking was estimated over his lifetime based on his responses to the 1997 questionnaire, with 1 pack-year defined as 365 packs of cigarettes smoked during a single year.

15.1.4 Statistical Methods

Table 15-1 summarizes the statistical analyses performed for the hematologic assessment. The first part of this table describes the dependent variables analyzed. The second part of this table provides a further description of the covariates examined. A covariate was used in its continuous form whenever possible for all adjusted analyses; if necessary, if the covariate is inherently discrete (e.g., military occupations), or if a categorized form was needed to develop measures of association with the dependent variables, the

covariate was categorized as shown in Table 15-1. Table 15-2 provides a summary of the number of participants with missing dependent variable and covariate data. In addition, the number of participants excluded because of medical conditions is given.

Table 15-1. Statistical Analysis for the Hematologic Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
RBC Count (million/mm^3)	LAB	D/C	Abnormal Low: <4.3 Normal: 4.3–5.9 Abnormal High: >5.9	(1)	(a)	U:PR,GLM A:PR,GLM
WBC Count (thousand/mm^3)	LAB	D/C	Abnormal Low: <4.5 Normal: 4.5–11.0 Abnormal High: >11.0	(1)	(a)	U:PR,GLM A:PR,GLM
Hemoglobin (gm/dl)	LAB	D/C	Abnormal Low: <13.9 Normal: 13.9–18.0 Abnormal High: >18.0	(1)	(a)	U:PR,GLM,CS A:PR,GLM
Hematocrit (percent)	LAB	D/C	Abnormal Low: <39.0 Normal: 39.0–55.0 Abnormal High: >55.0	(1)	(a)	U:PR,GLM,CS A:PR,GLM
Platelet Count (thousand/mm^3)	LAB	D/C	Abnormal Low: <130 Normal: 130–400 Abnormal High: >400	(1)	(a)	U:PR,GLM,CS A:PR,GLM L:PR,GLM
Prothrombin Time (seconds)	LAB	D/C	High: >12.3 Normal: ≤12.3	(1)	(b)	U:LR,GLM,CS A:LR,GLM
RBC Morphology	LAB	D	Abnormal Normal	(1)	(a)	U:LR A:LR
Absolute Neutrophils (segs) (thousand/mm^3)	LAB	C	--	(1)	(a)	U:GLM A:GLM
Absolute Neutrophils (bands) (thousand/mm^3)	LAB	D/C	Zero Nonzero	(1)	(a)	U:LR,GLM A:LR,GLM
Absolute Lymphocytes (thousand/mm^3)	LAB	C	--	(1)	(a)	U:GLM A:GLM
Absolute Monocytes (thousand/mm^3)	LAB	C	--	(1)	(a)	U:GLM A:GLM
Absolute Eosinophils (thousand/mm^3)	LAB	D/C	Zero Nonzero	(1)	(a)	U:LR,GLM A:LR,GLM
Absolute Basophils (thousand/mm^3)	LAB	D/C	Zero Nonzero	(1)	(a)	U:LR,GLM A:LR,GLM

[a]Covariates:
(1): age, race, military occupation, current cigarette smoking, lifetime cigarette smoking history.

Table 15-1. Statistical Analysis for the Hematologic Assessment (Continued)

[b]Exclusions:
(a): participants with body temperatures greater than or equal to 100° Fahrenheit, participants testing positive for HIV.
(b): participants testing positive for HIV, participants taking an anticoagulant (such as Coumadin®) or aspirin at the time of the examination.

Covariates

Variable (Units)	Data Source	Data Form	Cutpoints
Age (years)	MIL	D/C	Born ≥1942 Born <1942
Race	MIL	D	Black Non-Black
Occupation	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Current Cigarette Smoking (cigarettes/day)	Q-SR	D/C	0-Never 0-Former >0–20 >20
Lifetime Cigarette Smoking History (pack-years)	Q-SR	D/C	0 >0–10 >10

Abbreviations

Data Source: LAB: 1997 laboratory results
MIL: Air Force military records
Q-SR: Health questionnaires (self-reported)

Data Form: C: Continuous analysis only
D: Discrete analysis only
D/C: Discrete and continuous analyses for dependent variables; appropriate form for analysis (either discrete or continuous) for covariates

Statistical Analysis: U: Unadjusted analysis
A: Adjusted analysis
L: Longitudinal analysis

Statistical Methods: CS: Chi-square contingency table analysis (continuity-adjusted)
GLM: General linear models analysis
LR: Logistic regression analysis
PR: Polytomous logistic regression analysis

Table 15-2. Number of Participants Excluded or with Missing Data for the Hematology Assessment

Variable	Variable Use	Group: Ranch Hand	Group: Comparison	Dioxin (Ranch Hands Only): Initial	Dioxin (Ranch Hands Only): 1987	Categorized Dioxin: Ranch Hand	Categorized Dioxin: Comparison
Platelet Count	DEP	4	6	2	4	4	6
Prothrombin Time	DEP	0	1	0	0	0	1
Current Cigarette Smoking	COV	1	0	0	1	1	0
Lifetime Cigarette Smoking History	COV	2	1	1	2	2	1
Body Temperature ≥100° Fahrenheit at the Time of the Physical Exam	EXC	1	0	1	1	1	0
HIV Positive	EXC	3	2	3	3	3	2
Taking an Anticoagulant or Aspirin at the Time of the Physical Exam	EXC	179	232	104	176	176	223

Note: DEP = Dependent variable.
COV = Covariate.
EXC = Exclusion.
870 Ranch Hands and 1,251 Comparisons.
482 Ranch Hands for initial dioxin; 863 Ranch Hands for 1987 dioxin.
863 Ranch Hands and 1,213 Comparisons for categorized dioxin.

Absolute neutrophils (bands), absolute eosinophils, and absolute basophils had a large number of measurements equal to 0 counts per mm^3. The nonzero measurements exhibited a positively skewed distribution, and a logarithmic transformation, however, was applied to achieve an approximate normal distribution. The logarithmic transformation, however, could not be applied to the measurements equal to 0 counts per mm^3. Consequently, these variables were analyzed in two forms: (a) a continuous analysis of the nonzero measurements and (b) a discrete analysis of the proportion of zero measurements.

15.1.4.1 Longitudinal Analysis

Longitudinal analyses on platelet count were conducted to evaluate the association of exposure to mean changes between the 1982 baseline examination and the 1997 follow-up examination.

15.2 RESULTS

15.2.1 Dependent Variable-Covariate Associations

Tests of associations were performed for each dependent variable in the hematology assessment with each covariate. Results are displayed in Appendix F, Table F-7. These associations are pairwise between the dependent variable and the covariate and are not adjusted for any other covariates. Participants who tested positive for HIV or who had a body temperature greater than or equal to 100° Fahrenheit were excluded from the analysis of all variables except prothrombin time. The analysis of prothrombin time included all participants except those testing positive for HIV or those taking an anticoagulant or aspirin at the time of the examination. In addition, one participant had a hemolyzed specimen for prothrombin time and was excluded from the analysis of this variable.

RBC count in its continuous form displayed a significant association with age ($p<0.001$), occupation ($p<0.001$), current cigarette smoking ($p=0.003$), and lifetime cigarette smoking history ($p=0.031$). RBC count decreased as age increased ($r=-0.181$). Among the occupational strata, enlisted groundcrew displayed the highest mean RBC count (5.01 million/mm^3), followed by enlisted flyers (4.95 million/mm^3), then officers (4.90 million/mm^3). RBC count increased as current cigarette smoking increased ($r=0.064$). Conversely, as lifetime cigarette smoking increased, RBC count decreased ($r=-0.047$).

Tests of covariate associations involving RBC count in its discrete form revealed significant findings for age ($p=0.001$) and race ($p=0.001$). The prevalence of both low and high RBC abnormalities were higher among older participants and among Blacks.

Significant associations were found between WBC count in its continuous form and race ($p<0.001$), occupation ($p<0.001$), current cigarette smoking ($p<0.001$), and lifetime cigarette smoking history ($p<0.001$). Non-Blacks had a higher mean WBC count (6.71 thousand/mm^3) than did Blacks (5.94 thousand/mm^3). Enlisted groundcrew had the highest mean WBC count (6.91 thousand/mm^3), followed by enlisted flyers (6.80 thousand/mm^3), then officers (6.33 thousand/mm^3). The current cigarette smoking and lifetime cigarette smoking history associations were positive ($r=0.395$ and $r=0.236$, respectively), indicating WBC count increased as the level of current cigarette smoking and the level of lifetime cigarette smoking history increased.

Analysis of WBC count in its discrete form revealed significant associations with race ($p=0.001$), current cigarette smoking ($p=0.001$), and lifetime cigarette smoking history ($p=0.001$), and a marginally significant association with occupation ($p=0.056$). Blacks displayed a higher percentage of abnormally low WBC counts (18.8%) than did non-Blacks (4.5%), but a lower percentage of abnormally high WBC counts (2.3%) than non-Blacks (3.7%). Officers displayed the highest percentage of abnormally low WBC counts (6.1%), but the lowest percentage of abnormally high WBC counts (2.3%). Enlisted flyers had the lowest percentage of abnormally low WBC counts (4.7%), while also displaying the highest percentage of abnormally high WBC counts (5.3%). Participants who had never smoked displayed the highest percentage of abnormally low WBC count levels (7.9%). The percentage of abnormally low WBC counts decreased as current cigarette smoking levels increased. The converse was true for the percentage of abnormally high WBC count levels. Participants smoking more than 20 cigarettes per day had the highest percentage of abnormally high WBC counts (16.1%), while nonsmokers had the lowest (1.4%). The tests of association with lifetime cigarette smoking history were similar to current cigarette smoking. Participants who had never smoked had the highest percentage of abnormally low WBC counts (7.9%), while participants in the more than 10 pack-years category displayed the highest percentage of abnormally high WBC counts (5.3%).

Tests of associations with hemoglobin in its continuous form revealed significant results for age ($p<0.001$), race ($p<0.001$), and current cigarette smoking ($p<0.001$). The association with occupation was marginally significant ($p=0.076$). Hemoglobin levels decreased as age increased ($r=-0.137$). Non-Blacks had a higher hemoglobin mean (15.36 gm/dl) than Blacks (14.77 gm/dl), while the highest hemoglobin mean was found among enlisted groundcrew (15.37 gm/dl). Hemoglobin levels increased as current cigarette smoking levels increased ($r=0.213$).

Hemoglobin in its discrete form also showed significant associations with age ($p=0.002$), race ($p=0.001$), and current cigarette smoking ($p=0.031$). The percentage of abnormally low hemoglobin levels was higher among older participants (8.3%) than among younger participants (4.5%). Blacks displayed a higher percentage of abnormally low hemoglobin levels (17.2%) than non-Blacks (6.0%). Former cigarette smokers had the highest percentage of abnormally low hemoglobin levels (8.1%), whereas 2.2 percent of participants smoking more than an average of 20 cigarettes per day had abnormally low

hemoglobin levels. Participants who smoked no more than 20 cigarettes per day displayed the highest percentage of abnormally high hemoglobin levels (1.1%), while participants who had never smoked had the lowest percentage (0.3%).

Significant associations with hematocrit in its continuous form were observed for age ($p<0.001$), race ($p<0.001$), occupation ($p=0.050$), and current cigarette smoking ($p<0.001$). A marginally significant association was found with lifetime cigarette smoking history ($p=0.085$). Hematocrit levels decreased as age increased ($r=-0.121$). The mean level of hematocrit was 45.65 percent for non-Blacks, compared to 44.49 percent for Blacks. Within the occupational strata, mean levels of hematocrit were 45.38 percent, 45.62 percent, and 45.74 percent for officers, enlisted flyers, and enlisted groundcrew, respectively. Hematocrit levels increased as current cigarette smoking increased ($r=0.209$). Hematocrit levels increased as lifetime cigarette smoking levels increased ($r=0.037$).

Age was significantly associated with hematocrit in its discrete form ($p=0.014$). The percentage of abnormally low hematocrit levels was higher among older participants (3.2%) than among younger participants (1.3%). The percentage of abnormally high levels of hematocrit was 0.3 percent for older participants compared to 0.2 percent for younger participants.

Platelet count in its continuous form displayed significant associations with age ($p<0.001$), occupation ($p=0.015$), current cigarette smoking ($p=0.005$), and lifetime cigarette smoking history ($p<0.001$). Tests of association revealed that platelet count decreased as age increased ($r=-0.120$). Platelet count means were highest among enlisted groundcrew (208.2 thousand/mm^3), followed by enlisted flyers (205.5 thousand/mm^3), then officers (201.6 thousand/mm^3). Positive relations between platelet count and current cigarette smoking ($r=0.062$) and lifetime cigarette smoking history ($r=0.094$) indicated that platelet counts increased as the number of cigarettes per day and the number of pack-years increased, respectively.

Age was significantly associated with platelet count in its discrete form ($p=0.022$). Current cigarette smoking was marginally significantly associated with platelet count ($p=0.070$). The rate of abnormally low platelet counts was 3.7 percent among older participants and 1.9 percent among younger participants. The rate of abnormally high platelet counts was also higher among older participants (0.6%) than among younger participants (0.2%). Abnormally low platelet counts were most prevalent among participants who smoked no more than 20 cigarettes per day on average (3.4%). The highest percentage of abnormally high platelet counts was among participants smoking more than 20 cigarettes per day (2.2%).

Prothrombin time in its continuous form was significantly associated with age ($p<0.001$). Prothrombin time increased as age increased ($r=0.096$). The association was marginally significant between age and the discrete form of prothrombin time ($p=0.077$). A greater percentage of participants with abnormal (high) prothrombin times was observed in older participants (1.9%) than in younger participants (0.8%).

RBC morphology was significantly associated with age, race, current cigarette smoking, and lifetime cigarette smoking history ($p=0.013$, $p=0.001$, $p=0.001$, and $p=0.001$, respectively). The association between RBC morphology and occupation was marginally significant ($p=0.072$). Older participants and Blacks displayed the higher percentages of RBC morphology abnormalities (8.0% and 14.1%, respectively) as compared to younger participants and non-Blacks (5.2% and 6.3%, respectively). The RBC morphology abnormality rates increased as the levels of current cigarette smoking and lifetime cigarette smoking history each increased (3.7%, 7.3%, 9.7%, and 10.2% for the four current cigarette smoking categories and 3.7%, 7.0%, and 8.5% for the three lifetime cigarette smoking history categories). The percentages of abnormalities were 9.5 for enlisted flyers, 6.7 for enlisted groundcrew, and 5.8 for officers.

Examination of absolute neutrophils (segs) displayed significant covariate associations with race ($p<0.001$), occupation ($p<0.001$), current cigarette smoking ($p<0.001$), and lifetime cigarette smoking history ($p<0.001$). Mean absolute neutrophils (segs) levels were 3.88 thousand/mm^3 for non-Blacks and 3.13 thousand/mm^3 for Blacks. Within the occupational strata, mean absolute neutrophils (segs) levels were highest among enlisted groundcrew (4.00 thousand/mm^3), followed by enlisted flyers (3.94 thousand/mm^3), then officers (3.60 thousand/mm^3). Absolute neutrophils (segs) increased as current cigarette smoking and lifetime cigarette smoking increased ($r=0.347$ and $r=0.214$, respectively).

For participants with positive absolute neutrophil (bands) levels, significant covariate associations were seen with age ($p=0.003$), race ($p<0.001$), current cigarette smoking ($p<0.001$), and lifetime cigarette smoking history ($p<0.001$). The level of absolute neutrophil (bands) increased as age, current cigarette smoking, and lifetime cigarette smoking history increased ($r=0.071$ for age, $r=0.188$, for current cigarette smoking; $r=0.133$ for lifetime cigarette smoking history). The significant absolute neutrophil (bands) association with race revealed a mean of 0.200 thousand/mm^3 for non-Blacks and a mean of 0.120 thousand/mm^3 for Blacks. A significant association with race also was revealed when the percentage of participants with measurements of zero absolute neutrophils (bands) was examined ($p=0.032$). For Blacks, 24.2 percent had zero absolute neutrophils, whereas 16.5 percent of non-Blacks had zero absolute neutrophils.

Absolute lymphocytes were significantly associated with age ($p<0.001$), race ($p=0.035$), occupation ($p<0.001$), current cigarette smoking ($p<0.001$), and lifetime cigarette smoking history ($p=0.002$). Absolute lymphocyte levels decreased as age increased ($r=-0.116$). Blacks displayed higher mean absolute lymphocyte levels (1.87 thousand/mm^3) than did non-Blacks (1.75 thousand/mm^3). Mean levels of absolute lymphocytes for each occupational stratum were 1.82 thousand/mm^3 for enlisted groundcrew, 1.75 thousand/mm^3 for enlisted flyers, and 1.68 thousand/mm^3 for officers. Absolute lymphocyte levels increased as current cigarette smoking and lifetime cigarette smoking history increased ($r=0.195$ and $r=0.067$, respectively).

Results from the examination of covariate associations for absolute monocytes revealed significant associations with age ($p=0.043$), current cigarette smoking ($p<0.001$), and lifetime cigarette smoking history ($p<0.001$). Absolute monocyte levels increased as each of these covariates increased ($r=0.044$ for age, $r=0.160$ for current cigarette smoking, and $r=0.142$ for lifetime cigarette smoking history).

For participants with positive absolute eosinophil levels, significant associations were found between current cigarette smoking and lifetime cigarette smoking history ($p<0.001$ for each). Absolute eosinophils increased as current cigarette smoking and lifetime cigarette smoking history increased ($r=0.134$ and $r=0.086$, respectively). The percentage of participants with zero eosinophils was significantly associated with occupation ($p=0.005$). The percentages of participants with zero eosinophils were 14.7 for enlisted groundcrew, 11.5 for enlisted flyers, and 9.7 for officers.

Race, current cigarette smoking, and lifetime cigarette smoking history were significantly associated with basophils ($p=0.006$, $p<0.001$, and $p<0.001$, respectively) for participants whose absolute basophil level was positive. Mean levels of absolute basophils were 0.080 thousand/mm^3 for non-Blacks, compared to 0.068 thousand/mm^3 for Blacks. Basophils increased as current cigarette smoking and lifetime cigarette smoking history increased ($r=0.267$ and $r=0.168$, respectively). The proportion of participants with zero basophils was significantly associated with current cigarette smoking and lifetime cigarette smoking history ($p=0.033$ and $p=0.038$, respectively). Among levels of current cigarette smoking, the two highest percentages of participants with zero basophils were among participants who had never smoked (59.2%) and participants who were currently the heaviest smokers (59.9%). The percentage of participants with zero basophils decreased as the level of lifetime cigarette smoking history increased.

15.2.2 Exposure Analysis

The following section presents results of the statistical analyses of the dependent variables shown in Table 15-1. Dependent variables are derived from the laboratory portion of the 1997 follow-up examination.

Four models were examined for each dependent variable given in Table 15-1. The analyses of these models are presented below. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7, respectively. These analyses were performed both unadjusted and adjusted for relevant covariates. Model 1 examined the relation between the dependent variable and group (i.e., Ranch Hand or Comparison). In this model, exposure was defined as "yes" for Ranch Hands and "no" for Comparisons without regard to the magnitude of the exposure. As an attempt to quantify exposure, three contrasts of Ranch Hands and Comparisons were performed along with the overall Ranch Hand versus Comparison contrast. These three contrasts compared Ranch Hands and Comparisons within each occupational category (i.e., officers, enlisted flyers, and enlisted groundcrew). As described in previous reports and Table 2-8, the average levels of exposure to dioxin were highest for enlisted groundcrew, followed by enlisted flyers, then officers.

Model 2 explored the relation between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 parts per trillion (ppt). If a participant did not have a 1987 dioxin level, the 1992 level was used to estimate the initial dioxin level. If a participant did not have a 1987 or a 1992 dioxin level, the 1997 level was used to estimate the initial dioxin level. A statistical adjustment for the percentage of body fat at the time of the participant's blood measurement of dioxin is included in this model to account for body-fat-related differences in elimination rate (40).

Model 3 divided the Ranch Hands examined in Model 2 into two categories based on their initial dioxin measures. These two categories are referred to as "low Ranch Hand" and "high Ranch Hand." Two additional categories, Ranch Hands with 1987 serum dioxin levels at or below 10 ppt and Comparisons with 1987 serum dioxin levels at or below 10 ppt, were formed and included in the model. Ranch Hands with 1987 serum dioxin levels at or below 10 ppt are referred to as the "background Ranch Hand" category. Dioxin levels in 1992 were used if the 1987 level was not available, and dioxin levels in 1997 were used if the 1987 and 1992 levels were not available. These four categories—Comparisons, background Ranch Hands, low Ranch Hands, and high Ranch Hands—were used in Model 3 analyses. The relation between the dependent variable in each of the three Ranch Hand categories and the dependent variable in the "Comparison" category was examined. A fourth contrast, exploring the relation of the dependent variable in the combined low and high Ranch Hand categories relative to Comparisons, also was conducted. This combination is referred to in the tables as the "low plus high Ranch Hand" category. As in Model 2, a statistical adjustment for the percentage of body fat at the time of the participant's blood measurement of dioxin was included in this model.

Model 4 examined the relation between the dependent variable and 1987 lipid-adjusted dioxin levels in all Ranch Hands with a dioxin measurement. If a participant did not have a 1987 dioxin measurement, the 1992 measurement was used in determining the dioxin level. If a participant did not have a 1987 or a 1992 dioxin measurement, the 1997 measurement was used in determining the dioxin level.

15.2.2.1 *Laboratory Examination Variables*

15.2.2.1.1 *RBC Count (Continuous)*

The Model 3 unadjusted analysis of dioxin categories revealed a marginally significant difference between Ranch Hands in the low dioxin category and Comparisons. The mean RBC count was higher for Comparisons than for Ranch Hands in the low dioxin category (Table 15-3(e): p=0.094, difference of adjusted means=–0.05 million/mm^3). Other analyses of dioxin categories in Model 3 and analyses from Models 1, 2, and 4 were all nonsignificant (Table 15-3(a–h): p>0.10 for all other analyses).

Table 15-3. Analysis of RBC Count (million/mm^3) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean	Difference of Means (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***4.95***	***–0.02 (–0.05,0.02)***	***0.318***
	Comparison	***1,249***	***4.96***		
Officer	Ranch Hand	341	4.89	–0.03 (–0.09,0.02)	0.234
	Comparison	493	4.92		
Enlisted Flyer	Ranch Hand	151	4.92	–0.04 (–0.12,0.04)	0.333
	Comparison	187	4.97		
Enlisted Groundcrew	Ranch Hand	374	5.01	0.01 (–0.04,0.06)	0.753
	Comparison	569	5.00		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adjusted Mean	Difference of Adj. Means (95% C.I.)	p-Value
All	***Ranch Hand***	***864***	***4.95***	***–0.02 (–0.05,0.02)***	***0.311***
	Comparison	***1,248***	***4.96***		
Officer	Ranch Hand	340	4.91	–0.03 (–0.08,0.02)	0.268
	Comparison	493	4.94		
Enlisted Flyer	Ranch Hand	151	4.94	–0.04 (–0.12,0.04)	0.343
	Comparison	187	4.98		
Enlisted Groundcrew	Ranch Hand	373	4.98	0.00 (–0.05,0.05)	0.919
	Comparison	568	4.97		

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Mean[a]	Adj. Mean[a]	R^2	Slope (Std. Error)	p-Value
Low	160	4.91	4.91	0.019	0.023 (0.014)	0.102
Medium	162	4.97	4.97			
High	156	4.99	4.99			

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 15-3. Analysis of RBC Count (million/mm^3) (Continuous) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean	R^2	Adj. Slope (Std. Error)	p-Value
Low	159	4.96	0.070	–0.004 (0.016)	0.821
Medium	162	4.98			
High	156	4.96			

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,211	4.96	4.96		
Background RH	381	4.94	4.95	–0.01 (–0.06,0.03)	0.540
Low RH	239	4.92	4.92	–0.05 (–0.10,0.01)	0.094
High RH	239	4.99	4.98	0.02 (–0.04,0.07)	0.506
Low plus High RH	478	4.96	4.95	–0.01 (–0.05,0.03)	0.510

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,210	4.97		
Background RH	380	4.97	0.00 (–0.04,0.05)	0.893
Low RH	238	4.93	–0.03 (–0.09,0.02)	0.230
High RH	239	4.94	–0.02 (–0.08,0.03)	0.441
Low plus High RH	477	4.94	–0.03 (–0.07,0.01)	0.196

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-3. Analysis of RBC Count (million/mm³) (Continuous) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean	R^2	Slope (Std. Error)	p-Value
Low	288	4.94	0.003	0.013 (0.009)	0.136
Medium	287	4.92			
High	284	4.99			

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean	R^2	Adjusted Slope (Std. Error)	p-Value
Low	287	4.99	0.047	–0.001 (0.010)	0.941
Medium	286	4.96			
High	284	4.98			

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

15.2.2.1.2 RBC Count (Discrete)

All results from the analyses of RBC count in the discrete form were nonsignificant (Table 15-4(a–h): p>0.15 for each unadjusted and adjusted analysis of Models 1 through 4).

Table 15-4. Analysis of RBC Count (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal Low	Number (%) Normal	Number (%) Abnormal High	Abnormal Low vs. Normal Est. Relative Risk (95% C.I.)	Abnormal Low vs. Normal p-Value	Abnormal High vs. Normal Est. Relative Risk (95% C.I.)	Abnormal High vs. Normal p-Value
All	***Ranch Hand***	***866***	***42 (4.9)***	***818 (94.5)***	***6 (0.7)***	***1.01 (0.67,1.51)***	***0.979***	***0.62 (0.24,1.61)***	***0.322***
	Comparison	***1,249***	***60 (4.8)***	***1,175 (94.1)***	***14 (1.1)***				
Officer	Ranch Hand	341	19 (5.6)	321 (94.1)	1 (0.3)	0.97 (0.53,1.77)	0.921	0.24 (0.03,1.98)	0.185
	Comparison	493	28 (5.7)	459 (93.1)	6 (1.2)				
Enlisted Flyer	Ranch Hand	151	11 (7.3)	138 (91.4)	2 (1.3)	2.03 (0.77,5.36)	0.155	1.29 (0.18,9.27)	0.800
	Comparison	187	7 (3.7)	178 (95.2)	2 (1.1)				
Enlisted Groundcrew	Ranch Hand	374	12 (3.2)	359 (96.0)	3 (0.8)	0.72 (0.36,1.45)	0.357	0.75 (0.19,3.02)	0.685
	Comparison	569	25 (4.4)	538 (94.6)	6 (1.1)				

(b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Abnormal Low vs. Normal Adj. Relative Risk (95% C.I.)	Abnormal Low vs. Normal p-Value	Abnormal High vs. Normal Adj. Relative Risk (95% C.I.)	Abnormal High vs. Normal p-Value
All	***1.00 (0.66,1.51)***	***0.991***	***0.58 (0.22,1.54)***	***0.278***
Officer	0.95 (0.52,1.75)	0.869	0.23 (0.03,1.89)	0.170
Enlisted Flyer	1.97 (0.73,5.29)	0.180	1.25 (0.17,9.24)	0.830
Enlisted Groundcrew	0.75 (0.37,1.53)	0.426	0.73 (0.18,2.98)	0.660

Table 15-4. Analysis of RBC Count (Discrete) (Continued)

(c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED								
Initial Dioxin Category Summary Statistics					Analysis Results for Log_2 (Initial Dioxin)[a]			
		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Initial Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
Low	160	9 (5.6)	150 (93.8)	1 (0.6)	0.79 (0.53,1.15)	0.220	0.76 (0.36,1.59)	0.464
Medium	162	7 (4.3)	151 (93.2)	4 (2.5)				
High	156	5 (3.2)	151 (96.8)	0 (0.0)				

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Initial Dioxin)			
	Abnormal Low vs. Normal		Abnormal High vs. Normal	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
477	0.95 (0.64, 1.41)	0.804	0.88 (0.39, 1.99)	0.751

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race because of the sparse number of participants with an abnormal high RBC count.

Table 15-4. Analysis of RBC Count (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED								
		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[ab]	p-Value	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	55 (4.5)	1,142 (94.3)	14 (1.2)				
Background RH	381	19 (5.0)	361 (94.8)	1 (0.3)	1.09 (0.64,1.87)	0.757	0.26 (0.03,1.99)	0.195
Low RH	239	12 (5.0)	225 (94.1)	2 (0.8)	1.11 (0.58,2.10)	0.753	0.69 (0.15,3.06)	0.623
High RH	239	9 (3.8)	227 (95.0)	3 (1.3)	0.83 (0.40,1.70)	0.603	0.94 (0.26,3.33)	0.921
Low plus High RH	478	21 (4.4)	452 (94.6)	5 (1.1)	0.96 (0.57,1.61)	0.868	0.80 (0.28,2.30)	0.683

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
		Abnormal Low vs. Normal		Abnormal High vs. Normal	
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,210				
Background RH	380	1.07 (0.61,1.86)	0.818	0.25 (0.03,1.99)	0.192
Low RH	238	0.92 (0.48,1.78)	0.809	0.54 (0.12,2.48)	0.431
High RH	239	1.04 (0.49,2.23)	0.917	1.16 (0.31,4.42)	0.827
Low plus High RH	477	0.98 (0.57,1.68)	0.942	0.79 (0.27,2.33)	0.676

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-4. Analysis of RBC Count (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS — 1987 DIOXIN — UNADJUSTED

	1987 Dioxin Category Summary Statistics				Analysis Results for Log_2 (1987 Dioxin + 1)			
		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
1987 Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[a]	p-Value	Est. Relative Risk (95% C.I.)[a]	p-Value
Low	288	13 (4.5)	274 (95.1)	1 (0.4)	0.91 (0.73,1.14)	0.405	1.16 (0.69,1.95)	0.566
Medium	287	16 (5.6)	270 (94.1)	1 (0.4)				
High	284	11 (3.9)	269 (94.7)	4 (1.4)				

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS — 1987 DIOXIN — ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin + 1)			
	Abnormal Low vs. Normal		Abnormal High vs. Normal	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
857	0.91 (0.69,1.21)	0.511	1.10 (0.60,2.00)	0.764

[a] Relative risk for a twofold increase in 1987 dioxin.

15.2.2.1.3 WBC Count (Continuous)

Each Model 1 contrast examining WBC count differences between Ranch Hands and Comparison means was nonsignificant, with and without covariate adjustment (Table 15-5(a,b): p>0.35 for each contrast).

Table 15-5. Analysis of WBC Count (thousand/mm³) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***866***	***6.67***	***0.02 --***	***0.789***
	Comparison	***1,249***	***6.65***		
Officer	Ranch Hand	341	6.33	0.00 --	0.970
	Comparison	493	6.33		
Enlisted Flyer	Ranch Hand	151	6.72	–0.14 --	0.474
	Comparison	187	6.86		
Enlisted Groundcrew	Ranch Hand	374	6.97	0.11 --	0.358
	Comparison	569	6.86		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***864***	***6.26***	***0.00 --***	***0.974***
	Comparison	***1,248***	***6.26***		
Officer	Ranch Hand	340	6.03	0.00 --	0.972
	Comparison	493	6.03		
Enlisted Flyer	Ranch Hand	151	6.17	–0.14 --	0.377
	Comparison	187	6.31		
Enlisted Groundcrew	Ranch Hand	373	6.55	0.05 --	0.648
	Comparison	568	6.50		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 15-5. Analysis of WBC Count (thousand/mm³) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	160	6.48	6.50	0.022	0.019 (0.009)	0.035
Medium	162	6.91	6.92			
High	156	6.90	6.88			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of WBC count versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	159	6.08	0.213	0.008 (0.009)	0.414
Medium	162	6.29			
High	156	6.22			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of WBC count versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,211	6.64	6.64		
Background RH	381	6.53	6.57	–0.07 --	0.493
Low RH	239	6.57	6.56	–0.08 --	0.491
High RH	239	6.96	6.92	0.28 --	0.029
Low plus High RH	478	6.76	6.73	0.09 --	0.324

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-5. Analysis of WBC Count (thousand/mm^3) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,210	6.27		
Background RH	380	6.28	0.01 --	0.902
Low RH	238	6.18	–0.09 --	0.383
High RH	239	6.33	0.06 --	0.600
Low plus High RH	477	6.26	–0.01 --	0.831

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for $\log_2$ (1987 Dioxin +1)[b]		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	288	6.45	0.007	0.015 (0.006)	0.013
Medium	287	6.60			
High	284	6.95			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of WBC count versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for $\log_2$ (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	287	6.09	0.219	0.007 (0.006)	0.263
Medium	286	6.18			
High	284	6.32			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of WBC count versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

The Model 2 unadjusted analysis of WBC count revealed a significant positive association between WBC count in its continuous form and initial dioxin (Table 15-5(c): p=0.035, slope=0.019). After covariate adjustment, the relation was nonsignificant (Table 15-5(d): p=0.414).

The mean WBC count for Ranch Hands in the high dioxin category was significantly greater than Comparisons in the Model 3 unadjusted analysis of WBC count (Table 15-5(e): p=0.029, difference of adjusted means=0.28 thousand/mm^3). Other unadjusted contrasts were nonsignificant, as well as all contrasts in the adjusted analysis (Table 15-5(e,f): p>0.32 for all other contrasts).

A significant positive association between WBC count and 1987 dioxin levels was found in the Model 4 unadjusted analysis (Table 15-5(g): p=0.013, slope=0.015). The association was nonsignificant after adjustment for covariates (Table 15-5(h): p=0.263).

15.2.2.1.4 WBC Count (Discrete)

No significant differences were found between Ranch Hands and Comparisons in Model 1 unadjusted and adjusted analyses (Table 15-6(a,b): p≥0.15 for each contrast).

Both the unadjusted and adjusted Model 2 analyses revealed a significant inverse association between initial dioxin and abnormally low WBC counts (Table 15-6(c,d): p=0.012, Est. RR=0.59; p=0.043, Adj. RR=0.61, respectively). As initial dioxin increased, the percentage of abnormally low WBC counts decreased. Analyses of the associations between initial dioxin and the percentage of participants with abnormally high WBC counts were nonsignificant (Table 15-6(c,d): p>0.39 for each analysis).

A higher percentage of abnormally low WBC counts was found among Ranch Hands in the low dioxin category relative to Comparisons (Table 15-6(e): p=0.027, Est. RR=1.82). After adjustment for covariates, this result became marginally significant (Table 15-6(f): p=0.070, Adj. RR=1.67). No other differences in the percentage of abnormal WBC counts between Ranch Hands and Comparisons were found (Table 15-6(e,f): p>0.18 for each remaining contrast).

Table 15-6. Analysis of WBC Count (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal Low	Number (%) Normal	Number (%) Abnormal High	Abnormal Low vs. Normal: Est. Relative Risk (95% C.I.)	Abnormal Low vs. Normal: p-Value	Abnormal High vs. Normal: Est. Relative Risk (95% C.I.)	Abnormal High vs. Normal: p-Value
All	***Ranch Hand***	***866***	***51 (5.9)***	***784 (90.5)***	***31 (3.6)***	***1.20 (0.82,1.75)***	***0.353***	***1.00 (0.63,1.60)***	***0.988***
	Comparison	***1,249***	***62 (5.0)***	***1,142 (91.4)***	***45 (3.6)***				
Officer	Ranch Hand	341	22 (6.5)	312 (91.5)	7 (2.1)	1.10 (0.62,1.95)	0.747	0.85 (0.33,2.17)	0.727
	Comparison	493	29 (5.9)	452 (91.7)	12 (2.4)				
Enlisted Flyer	Ranch Hand	151	10 (6.6)	133 (88.1)	8 (5.3)	2.14 (0.76,6.05)	0.150	1.03 (0.40,2.68)	0.954
	Comparison	187	6 (3.2)	171 (91.4)	10 (5.4)				
Enlisted Groundcrew	Ranch Hand	374	19 (5.1)	339 (90.6)	16 (4.3)	1.08 (0.59,1.97)	0.809	1.07 (0.55,2.05)	0.850
	Comparison	569	27 (4.8)	519 (91.2)	23 (4.0)				

(b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Abnormal Low vs. Normal: Adj. Relative Risk (95% C.I.)	Abnormal Low vs. Normal: p-Value	Abnormal High vs. Normal: Adj. Relative Risk (95% C.I.)	Abnormal High vs. Normal: p-Value
All	***1.18 (0.80,1.74)***	***0.415***	***0.93 (0.58,1.51)***	***0.783***
Officer	1.10 (0.62,1.96)	0.754	0.91 (0.35,2.35)	0.843
Enlisted Flyer	2.12 (0.73,6.09)	0.165	0.99 (0.37,2.68)	0.985
Enlisted Groundcrew	1.03 (0.55,1.93)	0.923	0.93 (0.47,1.82)	0.822

Table 15-6. Analysis of WBC Count (Discrete) (Continued)

(c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED								
Initial Dioxin Category Summary Statistics					Analysis Results for Log₂ (Initial Dioxin)[a]			
		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Initial Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
Low	160	16 (10.0)	139 (86.9)	5 (3.1)	0.59 (0.39,0.89)	0.012	0.99 (0.69,1.43)	0.964
Medium	162	7 (4.3)	148 (91.4)	7 (4.3)				
High	156	3 (1.9)	147 (94.2)	6 (3.9)				

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED				
	Analysis Results for Log₂ (Initial Dioxin)			
	Abnormal Low vs. Normal		Abnormal High vs. Normal	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
477	0.61 (0.38,0.99)	0.043	0.83 (0.54,1.27)	0.395

[a] Relative risk for a twofold increase in initial dioxin.

Table 15-6. Analysis of WBC Count (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED								
		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[ab]	p-Value	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	59 (4.9)	1,109 (91.6)	43 (3.6)				
Background RH	381	25 (6.6)	344 (90.3)	12 (3.2)	1.22 (0.75,1.99)	0.426	0.86 (0.45,1.67)	0.664
Low RH	239	20 (8.4)	212 (88.7)	7 (2.9)	1.82 (1.07,3.10)	0.027	0.86 (0.38,1.94)	0.716
High RH	239	6 (2.5)	222 (92.9)	11 (4.6)	0.56 (0.24,1.32)	0.188	1.32 (0.67,2.61)	0.420
Low plus High RH	478	26 (5.4)	434 (90.8)	18 (3.8)	1.01 (0.59,1.73)	0.963	1.07 (0.60,1.89)	0.825

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.
Comparison: 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
		Abnormal Low vs. Normal		Abnormal High vs. Normal	
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,210				
Background RH	380	1.16 (0.70,1.93)	0.564	0.86 (0.43,1.71)	0.660
Low RH	238	1.67 (0.96,2.91)	0.070	0.82 (0.36,1.90)	0.650
High RH	239	0.64 (0.26,1.56)	0.326	1.09 (0.53,2.24)	0.825
Low plus High RH	477	1.03 (0.59,1.81)	0.907	0.95 (0.52,1.72)	0.855

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.
Comparison: 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

Table 15-6. Analysis of WBC Count (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS — 1987 DIOXIN — UNADJUSTED								
1987 Dioxin Category Summary Statistics					Analysis Results for Log_2 (1987 Dioxin + 1)			
		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
1987 Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[a]	p-Value	Est. Relative Risk (95% C.I.)[a]	p-Value
Low	288	19 (6.6)	261 (90.6)	8 (2.8)	0.78 (0.63,0.96)	0.020	0.99 (0.77,1.27)	0.957
Medium	287	24 (8.4)	254 (88.5)	9 (3.1)				
High	284	8 (2.8)	263 (92.6)	13 (4.6)				

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS — 1987 DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (1987 Dioxin + 1)			
	Abnormal Low vs. Normal		Abnormal High vs. Normal	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
857	0.76 (0.59,0.98)	0.032	0.93 (0.72,1.20)	0.570

[a] Relative risk for a twofold increase in 1987 dioxin.

Although the contrasts of Ranch Hands in the low dioxin category and Comparisons indicated an increased percentage of Ranch Hands with an abnormally low WBC count (8.4% vs. 4.9%), contrasts of Ranch Hands in the high dioxin category and Comparisons showed the opposite pattern. As shown in Table 15-6(e) and 15-6(f), a smaller percentage of Ranch Hands in the high dioxin category (2.5%) had an abnormally low WBC count than did Comparisons (4.9%). Because of these opposite patterns, the percentages of Ranch Hands in the low and high dioxin categories combined and Comparisons were nearly equal. Consequently, a dose-response pattern was not evident between abnormally low WBC counts and dioxin in the Model 3 analyses.

Similar to the Model 2 analysis, the Model 4 unadjusted analysis of WBC count displayed a significant inverse relation between 1987 dioxin levels and abnormally low WBC count (Table 15-6(g): p=0.020, Est. RR=0.78). The significant relation remained after adjustment for covariates (Table 15-6(h): p=0.032, Adj. RR=0.76). As 1987 dioxin increased, the percentage of abnormally low WBC counts decreased. The associations between abnormally high WBC counts and 1987 dioxin were nonsignificant (Table 15-6(g,h): p≥0.57 for the unadjusted and adjusted analyses).

15.2.2.1.5 Hemoglobin (Continuous)

No significant results were found in the Model 1 unadjusted and adjusted analyses of hemoglobin in its continuous form (Table 15-7(a,b): p>0.20 for all contrasts).

Table 15-7. Analysis of Hemoglobin (gm/dl) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean	Difference of Means (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***15.32***	***0.00 (–0.09,0.09)***	***0.979***
	Comparison	***1,249***	***15.33***		
Officer	Ranch Hand	341	15.23	–0.06 (–0.20,0.08)	0.389
	Comparison	493	15.29		
Enlisted Flyer	Ranch Hand	151	15.29	–0.08 (–0.30,0.13)	0.445
	Comparison	187	15.38		
Enlisted Groundcrew	Ranch Hand	374	15.42	0.09 (–0.05,0.22)	0.206
	Comparison	569	15.34		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean	Difference of Adj. Means (95% C.I.)	p-Value
All	***Ranch Hand***	***864***	***15.05***	***–0.01 (–0.09,0.08)***	***0.883***
	Comparison	***1,248***	***15.05***		
Officer	Ranch Hand	340	15.03	–0.05 (–0.18,0.09)	0.489
	Comparison	493	15.07		
Enlisted Flyer	Ranch Hand	151	15.02	–0.09 (–0.29,0.12)	0.422
	Comparison	187	15.10		
Enlisted Groundcrew	Ranch Hand	373	15.07	0.06 (–0.07,0.19)	0.356
	Comparison	568	15.01		

Table 15-7. Analysis of Hemoglobin (gm/dl) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Mean	Adj. Mean[a]	R^2	Slope (Std. Error)	p-Value
Low	160	15.21	15.21	0.011	0.078 (0.034)	0.023
Medium	162	15.34	15.34			
High	156	15.52	15.52			

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean	R^2	Adj. Slope (Std. Error)	p-Value
Low	159	15.10	0.084	0.030 (0.039)	0.443
Medium	162	15.16			
High	156	15.28			

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,211	15.33	15.33		
Background RH	381	15.31	15.30	–0.03 (–0.14,0.09)	0.641
Low RH	239	15.26	15.26	–0.07 (–0.21,0.07)	0.319
High RH	239	15.45	15.46	0.12 (–0.01,0.26)	0.080
Low plus High RH	478	15.36	15.36	0.03 (–0.08,0.13)	0.617

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-7. Analysis of Hemoglobin (gm/dl) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,210	15.06		
Background RH	380	15.04	–0.02 (–0.14,0.09)	0.679
Low RH	238	15.04	–0.02 (–0.16,0.11)	0.731
High RH	239	15.12	0.06 (–0.08,0.20)	0.379
Low plus High RH	477	15.08	0.02 (–0.08,0.12)	0.715

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean	R^2	Slope (Std. Error)	p-Value
Low	288	15.34	0.003	0.035 (0.023)	0.133
Medium	287	15.22			
High	284	15.45			

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	287	15.13	0.088	0.021 (0.026)	0.421
Medium	286	15.06			
High	284	15.19			

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

A significant positive association between hemoglobin and initial dioxin was found in the unadjusted Model 2 analysis (Table 15-7(c): p=0.023, slope=0.078). The association was nonsignificant after adjustment for covariates (Table 15-7(d): p=0.443).

The Model 3 unadjusted analysis revealed a marginally significant higher mean hemoglobin level for Ranch Hands in the high dioxin category than for Comparisons (Table 15-7(e): p=0.080, difference of adjusted means=0.12 gm/dl). All other unadjusted contrasts were nonsignificant (Table 15-7(e): p>0.31 for all other contrasts). The contrast between Ranch Hands in the high dioxin category and Comparisons, as well as all other adjusted analysis contrasts, was nonsignificant (Table 15-7(f): p>0.37 for all adjusted contrasts).

The unadjusted and adjusted Model 4 analyses of hemoglobin revealed no significant associations with dioxin (Table 15-7(g,h): $p>0.13$ for both analyses).

15.2.2.1.6 Hemoglobin (Discrete)

Model 1 and Model 3 analyses of hemoglobin in its discrete form found no significant difference between Ranch Hands and Comparisons with respect to hemoglobin abnormalities (Table 15-8(a,b,e,f): $p>0.11$ for each unadjusted and adjusted contrast).

The Model 2 unadjusted analysis of hemoglobin revealed a marginally significant inverse association between initial dioxin and abnormally low hemoglobin levels (Table 15-8(c): $p=0.075$, Est. RR=0.74). After adjustment for covariates, the association was nonsignificant (Table 15-8(d): $p=0.364$). The association between abnormally high hemoglobin levels and initial dioxin was nonsignificant for both unadjusted and adjusted analyses (Table 15-8(c,d): $p>0.85$ for both analyses).

Table 15-8. Analysis of Hemoglobin (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal Low	Number (%) Normal	Number (%) Abnormal High	Abnormal Low vs. Normal: Est. Relative Risk (95% C.I.)	Abnormal Low vs. Normal: p-Value	Abnormal High vs. Normal: Est. Relative Risk (95% C.I.)	Abnormal High vs. Normal: p-Value
All	***Ranch Hand***	***866***	***62 (7.2)***	***801 (92.5)***	***3 (0.4)***	***1.14 (0.81,1.61)***	***0.458***	***0.62 (0.16,2.41)***	***0.493***
	Comparison	***1,249***	***79 (6.3)***	***1,163 (93.1)***	***7 (0.6)***				
Officer	Ranch Hand	341	25 (7.3)	314 (92.1)	2 (0.6)	1.27 (0.73,2.21)	0.400	1.47 (0.21,10.49)	0.700
	Comparison	493	29 (5.9)	462 (93.7)	2 (0.4)				
Enlisted Flyer	Ranch Hand	151	16 (10.6)	134 (88.7)	1 (0.7)	1.60 (0.74,3.44)	0.230	--	0.899[a]
	Comparison	187	13 (7.0)	174 (93.1)	0 (0.0)				
Enlisted Groundcrew	Ranch Hand	374	21 (5.6)	353 (94.4)	0 (0.0)	0.85 (0.49,1.47)	0.557	--	0.171[a]
	Comparison	569	37 (6.5)	527 (92.6)	5 (0.9)				

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormal high hemoglobin level.

--: Results not presented because of the sparse number of participants with an abnormal high hemoglobin level.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Abnormal Low vs. Normal: Adj. Relative Risk (95% C.I.)	Abnormal Low vs. Normal: p-Value	Abnormal High vs. Normal: Adj. Relative Risk (95% C.I.)	Abnormal High vs. Normal: p-Value
All	***1.15 (0.81,1.63)***	***0.433***	***0.61 (0.16,2.38)***	***0.480***
Officer	1.25 (0.72,2.19)	0.433	1.52 (0.21,10.95)	0.675
Enlisted Flyer	1.58 (0.73,3.44)	0.246	--	--
Enlisted Groundcrew	0.90 (0.51,1.58)	0.713	--	--

--: Results not presented because of the sparse number of participants with an abnormal high hemoglobin level.

Note: Results are not adjusted for race because of the sparse number of participants with an abnormal high hemoglobin level.

Table 15-8. Analysis of Hemoglobin (Discrete) (Continued)

(c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED								
	Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[a]			
		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Initial Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
Low	160	13 (8.1)	147 (91.9)	0 (0.0)	0.74 (0.53,1.03)	0.075	1.16 (0.24,5.60)	0.856
Medium	162	11 (6.8)	150 (92.6)	1 (0.6)				
High	156	5 (3.2)	151 (96.8)	0 (0.0)				

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Initial Dioxin)			
	Abnormal Low vs. Normal		Abnormal High vs. Normal	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
477	0.85 (0.61,1.20)	0.364	1.04 (0.17,6.53)	0.966

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for occupation or race because of the sparse number of participants with an abnormal high hemoglobin level.

Table 15-8. Analysis of Hemoglobin (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED								
		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[ab]	p-Value	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	74 (6.1)	1,130 (93.3)	7 (0.6)				
Background RH	381	30 (7.9)	349 (91.6)	2 (0.5)	1.35 (0.86,2.10)	0.188	1.04 (0.21,5.12)	0.958
Low RH	239	16 (6.7)	223 (93.3)	0 (0.0)	1.09 (0.62,1.90)	0.767	--	0.507[c]
High RH	239	13 (5.4)	225 (94.1)	1 (0.4)	0.86 (0.47,1.58)	0.630	0.64 (0.08,5.28)	0.677
Low plus High RH	478	29 (6.1)	448 (93.7)	1 (0.2)	0.97 (0.62,1.51)	0.887	--	0.547[c]

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormal high hemoglobin level.
--: Results not presented because of the sparse number of participants with an abnormal high hemoglobin level.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-8. Analysis of Hemoglobin (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
		Abnormal Low vs. Normal		Abnormal High vs. Normal	
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,210				
Background RH	380	1.44 (0.91,2.29)	0.118	1.01 (0.20,5.14)	0.987
Low RH	238	0.96 (0.54,1.70)	0.886	--	--
High RH	239	0.90 (0.48,1.69)	0.735	0.69 (0.08,6.00)	0.735
Low plus High RH	477	0.93 (0.59,1.47)	0.746	--	--

[a] Relative risk and confidence interval relative to Comparisons.

--: Results not presented because of the sparse number of participants with an abnormal high hemoglobin level.

Note: RH = Ranch Hand. Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt. Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for race because of the sparse number of participants with an abnormal high hemoglobin level.

(g) MODEL 4: RANCH HANDS — 1987 DIOXIN — UNADJUSTED								
	1987 Dioxin Category Summary Statistics				Analysis Results for Log_2 (1987 Dioxin + 1)			
		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
1987 Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[a]	p-Value	Est. Relative Risk (95% C.I.)[a]	p-Value
Low	288	21 (7.3)	265 (92.0)	2 (0.7)	0.82 (0.68,1.00)	0.049	0.47 (0.20,1.14)	0.096
Medium	287	23 (8.0)	264 (92.0)	0 (0.0)				
High	284	15 (5.3)	268 (94.4)	1 (0.4)				

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 15-8. Analysis of Hemoglobin (Discrete) (Continued)

(h) MODEL 4: RANCH HANDS — 1987 DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (1987 Dioxin + 1)			
	Abnormal Low vs. Normal		Abnormal High vs. Normal	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
857	0.84 (0.68,1.04)	0.108	0.52 (0.22,1.23)	0.135

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for occupation or race because of the sparse number of participants with an abnormal high hemoglobin level.

The Model 4 unadjusted analysis revealed a significant inverse association between abnormally low hemoglobin levels and 1987 dioxin levels (Table 15-8(g): p=0.049, Est. RR=0.82). In addition, a marginally significant inverse association between abnormally high hemoglobin levels and 1987 dioxin levels was found in the unadjusted analysis (Table 15-8(g): p=0.096, Est. RR=0.47). After adjustment for covariates, the association became nonsignificant (p>0.10 for each analysis).

15.2.2.1.7 Hematocrit (Continuous)

The Model 2 analysis of hematocrit in its continuous form revealed a significant positive association between hemoglobin and initial dioxin (Table 15-9(c): p=0.021, slope=0.241). After adjustment for covariates, the relation was nonsignificant (Table 15-9(d): p=0.443). All other analyses were nonsignificant (Table 15-9(a–h): p>0.14 for all other analyses).

Table 15-9. Analysis of Hematocrit (percent) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean	Difference of Means (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***45.56***	***–0.04 (–0.31,0.24)***	***0.798***
	Comparison	***1,249***	***45.59***		
Officer	Ranch Hand	341	45.24	–0.24 (–0.67,0.19)	0.274
	Comparison	493	45.48		
Enlisted Flyer	Ranch Hand	151	45.49	–0.23 (–0.90,0.44)	0.504
	Comparison	187	45.72		
Enlisted Groundcrew	Ranch Hand	374	45.88	0.22 (–0.18,0.63)	0.279
	Comparison	569	45.65		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean	Difference of Adj. Means (95% C.I.)	p-Value
All	***Ranch Hand***	***864***	***44.99***	***–0.06 (–0.32,0.21)***	***0.681***
	Comparison	***1,248***	***45.05***		
Officer	Ranch Hand	340	44.90	–0.21 (–0.63,0.21)	0.326
	Comparison	493	45.11		
Enlisted Flyer	Ranch Hand	151	44.92	–0.24 (–0.88,0.41)	0.477
	Comparison	187	45.16		
Enlisted Groundcrew	Ranch Hand	373	45.08	0.15 (–0.25,0.55)	0.457
	Comparison	568	44.93		

Table 15-9. Analysis of Hematocrit (percent) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Mean	Adj. Mean[a]	R^2	Slope (Std. Error)	p-Value
Low	160	45.17	45.17	0.011	0.241 (0.104)	0.021
Medium	162	45.58	45.58			
High	156	46.08	46.09			

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean	R^2	Adj. Slope (Std. Error)	p-Value
Low	159	45.06	0.068	0.091 (0.119)	0.443
Medium	162	45.26			
High	156	45.57			

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,211	45.61	45.61		
Background RH	381	45.57	45.56	–0.06 (–0.41,0.30)	0.756
Low RH	239	45.30	45.30	–0.31 (–0.74,0.12)	0.153
High RH	239	45.92	45.93	0.32 (–0.11,0.75)	0.147
Low plus High RH	478	45.61	45.61	0.00 (–0.32,0.33)	0.987

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-9. Analysis of Hematocrit (percent) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	**n**	**Adj. Mean**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)**	**p-Value**
Comparison	1,210	45.08		
Background RH	380	45.04	–0.04 (–0.39,0.32)	0.839
Low RH	238	44.87	–0.21 (–0.63,0.20)	0.318
High RH	239	45.22	0.14 (–0.29,0.56)	0.534
Low plus High RH	477	45.04	–0.04 (–0.36,0.28)	0.817

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin +1)**		
1987 Dioxin	**n**	**Mean**	**R^2**	**Slope (Std. Error)**	**p-Value**
Low	288	45.68	0.001	0.077 (0.071)	0.278
Medium	287	45.20			
High	284	45.89			

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**		
1987 Dioxin	**n**	**Adj. Mean[a]**	**R^2**	**Adjusted Slope (Std. Error)[b]**	**p-Value**
Low	287	45.40	0.075	0.029 (0.079)	0.712
Medium	286	45.01			
High	284	45.42			

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

15.2.2.1.8 Hematocrit (Discrete)

Analyses of hematocrit in its discrete form revealed no significant differences for Models 1 through 4 (Table 15-10(a–h): p>0.24 for each analysis performed).

Table 15-10. Analysis of Hematocrit (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal Low	Number (%) Normal	Number (%) Abnormal High	Abnormal Low vs. Normal: Est. Relative Risk (95% C.I.)	Abnormal Low vs. Normal: p-Value	Abnormal High vs. Normal: Est. Relative Risk (95% C.I.)	Abnormal High vs. Normal: p-Value
All	***Ranch Hand***	***866***	***21 (2.4)***	***844 (97.5)***	***1 (0.1)***	***1.04 (0.59,1.84)***	***0.886***	***0.29 (0.03,2.47)***	***0.256***
	Comparison	***1,249***	***29 (2.3)***	***1,215 (97.3)***	***5 (0.4)***				
Officer	Ranch Hand	341	8 (2.4)	333 (97.7)	0 (0.0)	0.96 (0.39,2.37)	0.928	--	0.647[a]
	Comparison	493	12 (2.4)	479 (97.2)	2 (0.4)				
Enlisted Flyer	Ranch Hand	151	6 (4.0)	144 (95.4)	1 (0.7)	1.91 (0.53,6.88)	0.325	--	0.907[a]
	Comparison	187	4 (2.1)	183 (97.9)	0 (0.0)				
Enlisted Groundcrew	Ranch Hand	374	7 (1.9)	367 (98.1)	0 (0.0)	0.81 (0.32,2.05)	0.659	--	0.413[a]
	Comparison	569	13 (2.3)	553 (97.2)	3 (0.5)				

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormal high hematocrit level.

--: Results not presented because of the sparse number of participants with an abnormal high hematocrit level.

Table 15-10. Analysis of Hematocrit (Discrete) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED				
	Abnormal Low vs. Normal		Abnormal High vs. Normal	
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Adj. Relative Risk (95% C.I.)	p-Value
All	***1.04 (0.59,1.85)***	***0.886***	***0.28 (0.03,2.40)***	***0.245***
Officer	0.95 (0.38,2.36)	0.908	--	--
Enlisted Flyer	1.84 (0.51,6.72)	0.353	--	--
Enlisted Groundcrew	0.85 (0.33,2.18)	0.739	--	--

--: Results not presented because of the sparse number of participants with an abnormal high hematocrit level.

Note: Results are not adjusted for race because of the sparse number of participants with an abnormal high hematocrit level.

(c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED								
Initial Dioxin Category Summary Statistics					Analysis Results for Log_2 (Initial Dioxin)[a]			
		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Initial Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
Low	160	3 (1.9)	157 (98.1)	0 (0.0)	0.95 (0.58,1.57)	0.840	1.17 (0.24,5.66)	0.841
Medium	162	5 (3.1)	156 (96.3)	1 (0.6)				
High	156	2 (1.3)	154 (98.7)	0 (0.0)				

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 15-10. Analysis of Hematocrit (Discrete) (Continued)

(d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Initial Dioxin)			
	Abnormal Low vs. Normal		Abnormal High vs. Normal	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
477	1.10 (0.66,1.85)	0.714	1.07 (0.17,6.61)	0.942

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race or occupation because of the sparse number of participants with an abnormal high hematocrit level.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED								
		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[ab]	p-Value	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	27 (2.2)	1,179 (97.4)	5 (0.4)				
Background RH	381	8 (2.1)	373 (97.9)	0 (0.0)	0.97 (0.43,2.16)	0.933	--	0.464[c]
Low RH	239	5 (2.1)	234 (97.9)	0 (0.0)	0.93 (0.35,2.43)	0.875	--	0.695[c]
High RH	239	5 (2.1)	233 (97.5)	1 (0.4)	0.91 (0.35,2.40)	0.850	0.91 (0.10,7.96)	0.931
Low plus High RH	478	10 (2.1)	467 (97.7)	1 (0.2)	0.92 (0.44,1.92)	0.820	--	0.856[c]

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormal high hematocrit level
--: Results not presented because of the sparse number of participants with an abnormal high hematocrit level.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-10. Analysis of Hematocrit (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
		Abnormal Low vs. Normal		Abnormal High vs. Normal	
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,210				
Background RH	380	1.00 (0.44,2.28)	0.998	--	--
Low RH	238	0.78 (0.29,2.07)	0.615	--	--
High RH	239	1.01 (0.37,2.77)	0.980	0.98 (0.10,9.53)	0.986
Low plus High RH	477	0.89 (0.42,1.89)	0.757	--	--

[a] Relative risk and confidence interval relative to Comparisons.
--: Results not presented because of the sparse number of participants with an abnormal high hematocrit level.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.
Comparison: 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

Results are not adjusted for race because of the sparse number of participants with an abnormal high hematocrit level.

(g) MODEL 4: RANCH HANDS — 1987 DIOXIN — UNADJUSTED								
1987 Dioxin Category Summary Statistics					Analysis Results for Log_2 (1987 Dioxin + 1)			
		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
1987 Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[a]	p-Value	Est. Relative Risk (95% C.I.)[a]	p-Value
Low	288	7 (2.4)	281 (97.6)	0 (0.0)	0.91 (0.65,1.26)	0.568	1.41 (0.43,4.63)	0.573
Medium	287	4 (1.4)	283 (98.6)	0 (0.0)				
High	284	7 (2.5)	276 (97.2)	1 (0.4)				

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 15-10. Analysis of Hematocrit (Discrete) (Continued)

(h) MODEL 4: RANCH HANDS — 1987 DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (1987 Dioxin + 1)			
	Abnormal Low vs. Normal		Abnormal High vs. Normal	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
857	0.97 (0.67,1.42)	0.894	1.44 (0.38,5.40)	0.588

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results not adjusted for race or occupation because of the sparse number of participants with an abnormal high hematocrit level.

15.2.2.1.9 Platelet Count (Continuous)

When Ranch Hands and Comparisons were examined across all occupations, the difference in mean platelet count between the groups was nonsignificant in both unadjusted and adjusted analyses (Table 15-11(a,b): $p \geq 0.15$ in both analyses). In both the unadjusted and adjusted analyses, significant differences in mean platelet counts were found between Ranch Hands and Comparisons within each occupational stratum (Table 15-11(a,b): $p \leq 0.014$ for all occupational strata in both unadjusted and adjusted analyses). Mean platelet counts were higher among Comparisons than among Ranch Hands for the officer stratum and higher among Ranch Hands than among Comparisons for the enlisted flyer and enlisted groundcrew strata.

Table 15-11. Analysis of Platelet Count (thousand/mm^3) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***862***	***207.0***	***3.1 --***	***0.150***
	Comparison	***1,243***	***203.9***		
Officer	Ranch Hand	338	196.6	–8.5 --	0.012
	Comparison	490	205.1		
Enlisted Flyer	Ranch Hand	151	213.8	14.9 --	0.005
	Comparison	185	198.8		
Enlisted Groundcrew	Ranch Hand	373	213.9	9.3 --	0.004
	Comparison	568	204.6		

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***860***	***205.8***	***2.9 --***	***0.172***
	Comparison	***1,242***	***203.0***		
Officer	Ranch Hand	337	199.1	–8.2 --	0.014
	Comparison	490	207.3		
Enlisted Flyer	Ranch Hand	151	213.3	15.6 --	0.003
	Comparison	185	197.7		
Enlisted Groundcrew	Ranch Hand	372	208.9	8.1 --	0.011
	Comparison	567	200.8		

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

Table 15-11. Analysis of Platelet Count (thousand/mm^3) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	159	204.2	203.8	0.016	0.145 (0.057)	0.012
Medium	162	208.0	207.9			
High	155	217.8	218.2			

[a] Transformed from square root scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on square root of platelet count versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	158	207.5	0.090	0.073 (0.065)	0.262
Medium	162	207.6			
High	155	214.7			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of platelet count versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,205	204.5	204.6		
Background RH	379	203.6	202.1	–2.5 --	0.374
Low RH	238	204.2	204.6	–0.1 --	0.987
High RH	238	215.7	217.2	12.6 --	<0.001
Low plus High RH	476	209.9	210.8	6.2 --	0.017

[a] Transformed from square root scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[d] P-value is based on difference of means on square root scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-11. Analysis of Platelet Count (thousand/mm^3) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,204	204.2		
Background RH	378	202.3	−1.9 --	0.509
Low RH	237	204.4	0.2 --	0.959
High RH	238	214.8	10.6 --	0.002
Low plus High RH	475	209.6	5.4 --	0.038

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)[b]		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	288	203.1	0.009	0.109 (0.039)	0.005
Medium	284	203.9			
High	283	214.5			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of platelet count versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	287	205.1	0.066	0.049 (0.044)	0.264
Medium	283	204.7			
High	283	209.1			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of platelet count versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

The Model 2 unadjusted analysis of platelet count in its continuous form revealed a significant positive association with initial dioxin (Table 15-11(c): p=0.012, slope=0.145). After adjustment for the effects of covariates, the association was nonsignificant (Table 15-11(d): p=0.262).

Unadjusted and adjusted Model 3 analyses of mean platelet count levels were significantly greater for Ranch Hands in the high dioxin category than for Comparisons (Table 15-11(e,f): difference of adjusted means=12.6 thousand/mm^3, p<0.001, for the unadjusted analysis; difference of adjusted means=10.6 thousand/mm^3, p=0.002, for the adjusted analysis). Mean platelet counts also were significantly greater for Ranch Hands in the low and high dioxin categories combined than for Comparisons (Table 15-11(e,f): difference of adjusted means=6.2 thousand/mm^3, p=0.017, for the unadjusted analysis; difference of adjusted means=5.4 thousand/mm^3, p=0.038, for the adjusted analysis). Although the mean difference increased as dioxin levels increased, other contrasts of Ranch Hands and Comparisons were nonsignificant (Table 15-11(e,f): p>0.37 for all remaining contrasts).

Similar to the Model 2 analysis, the Model 4 unadjusted analysis of platelet count in its continuous form revealed a significant positive association with the 1987 dioxin levels (Table 15-11(g): p=0.005, slope=0.109). The relation was nonsignificant after adjustment for covariates (Table 15-11(h): p=0.264).

15.2.2.1.10 Platelet Count (Discrete)

A significant difference in the percentage of participants with abnormally low platelet counts was observed between Ranch Hand and Comparison officers in both the unadjusted and adjusted analyses (Table 15-12(a,b): p=0.021, Est. RR=2.65; p=0.022, Adj. RR=2.64, respectively). A significant difference in the percentage of participants with abnormally low platelet counts also was found for enlisted flyers (Table 15-12(a,b): p=0.032, Est. RR=0.11; p=0.029, Adj. RR=0.10, for the unadjusted and adjusted analyses, respectively). More Ranch Hand than Comparison officers had abnormally low platelet counts, (4.7% vs. 1.8%), whereas more Comparison than Ranch Hand enlisted flyers exhibited abnormally low platelet counts (6.0 vs. 0.7%). Contrasts of all Ranch Hands versus all Comparisons, as well as Ranch Hand versus Comparison enlisted groundcrew, were nonsignificant (Table 15-12(a,b): p>0.11 for all contrasts).

No significant associations were seen between abnormal platelet counts and initial dioxin in the Model 2 analyses (p>0.15 for all analyses). The Model 3 contrasts of Ranch Hands in the high dioxin category with Comparisons revealed marginally significant differences, with a higher percentage of Comparisons having abnormal platelet counts (Table 15-12(e,f): p=0.067, Est. RR=0.26; p=0.068, Adj. RR=0.26, for the unadjusted and adjusted analyses, respectively). This same pattern was observed when Ranch Hands in the low and high categories combined were contrasted with Comparisons (Table 15-12(e,f): p=0.090, Est. RR=0.47; p=0.078, Adj. RR=0.45, for the unadjusted and adjusted analyses, respectively). All other Model 3 contrasts were nonsignificant (Table 15-12(e,f): p>0.21 for all remaining contrasts).

A significant association between 1987 dioxin levels and abnormally low platelet count measures was found in the Model 4 unadjusted analysis of platelet count (Table 15-12(g): p=0.028, Est. RR=0.70). These results were nonsignificant after adjustment for covariates (Table 15-12(h): p=0.135). Other analyses of abnormal platelet counts with 1987 dioxin were nonsignificant (Table 15-12(g,h): p>0.61 for all other analyses).

Table 15-12. Analysis of Platelet Count (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal Low	Number (%) Normal	Number (%) Abnormal High	Abnormal Low vs. Normal Est. Relative Risk (95% C.I.)	Abnormal Low vs. Normal p-Value	Abnormal High vs. Normal Est. Relative Risk (95% C.I.)	Abnormal High vs. Normal p-Value
All	***Ranch Hand***	***862***	***23 (2.7)***	***835 (96.9)***	***4 (0.5)***	***0.85 (0.50,1.43)***	***0.533***	***1.15 (0.31,4.29)***	***0.837***
	Comparison	***1,243***	***39 (3.1)***	***1,199 (96.5)***	***5 (0.4)***				
Officer	Ranch Hand	338	16 (4.7)	321 (95.0)	1 (0.3)	2.65 (1.16,6.06)	0.021	0.50 (0.05,4.79)	0.545
	Comparison	490	9 (1.8)	478 (97.6)	3 (0.6)				
Enlisted Flyer	Ranch Hand	151	1 (0.7)	149 (98.7)	1 (0.7)	0.11 (0.01,0.83)	0.032	1.16 (0.07,18.72)	0.916
	Comparison	185	11 (6.0)	173 (93.5)	1 (0.5)				
Enlisted Groundcrew	Ranch Hand	373	6 (1.6)	365 (97.9)	2 (0.5)	0.47 (0.19,1.20)	0.115	3.00 (0.27,33.23)	0.370
	Comparison	568	19 (3.4)	548 (96.5)	1 (0.2)				

(b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Abnormal Low vs. Normal Adj. Relative Risk (95% C.I.)	Abnormal Low vs. Normal p-Value	Abnormal High vs. Normal Adj. Relative Risk (95% C.I.)	Abnormal High vs. Normal p-Value
All	***0.84 (0.50,1.42)***	***0.509***	***1.13 (0.30,4.27)***	***0.853***
Officer	2.64 (1.15,6.05)	0.022	0.55 (0.06,5.37)	0.606
Enlisted Flyer	0.10 (0.01,0.79)	0.029	1.18 (0.07,19.42)	0.906
Enlisted Groundcrew	0.48 (0.19,1.23)	0.127	2.61 (0.23,29.36)	0.437

Table 15-12. *Analysis of Platelet Count (Discrete) (Continued)*

(c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category	Initial Dioxin Category Summary Statistics: n	Number (%): Abnormal Low	Number (%): Normal	Number (%): Abnormal High	Analysis Results for Log_2 (Initial Dioxin)[a] — Abnormal Low vs. Normal: Est. Relative Risk (95% C.I.)[b]	Abnormal Low vs. Normal: p-Value	Abnormal High vs. Normal: Est. Relative Risk (95% C.I.)[b]	Abnormal High vs. Normal: p-Value
Low	159	3 (1.9)	156 (98.1)	0 (0.0)	0.63 (0.33,1.19)	0.152	1.28 (0.49,3.36)	0.616
Medium	162	4 (2.5)	157 (96.9)	1 (0.6)				
High	155	1 (0.7)	153 (98.7)	1 (0.7)				

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

n	Analysis Results for Log_2 (Initial Dioxin) — Abnormal Low vs. Normal: Adj. Relative Risk (95% C.I.)[a]	Abnormal Low vs. Normal: p-Value	Abnormal High vs. Normal: Adj. Relative Risk (95% C.I.)[a]	Abnormal High vs. Normal: p-Value
475	0.69 (0.35,1.37)	0.290	0.67 (0.16,2.88)	0.590

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for occupation and race because of the sparse number of participants with an abnormal high platelet count.

Table 15-12. Analysis of Platelet Count (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED								
		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[ab]	p-Value	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,205	35 (2.9)	1,165 (96.7)	5 (0.4)				
Background RH	379	14 (3.7)	363 (95.8)	2 (0.5)	1.40 (0.74,2.66)	0.299	1.02 (0.19,5.30)	0.984
Low RH	238	6 (2.5)	232 (97.5)	0 (0.0)	0.84 (0.35,2.03)	0.702	--	0.693[c]
High RH	238	2 (0.8)	234 (98.3)	2.(0.8)	0.26 (0.06,1.10)	0.067	2.61 (0.49,13.84)	0.261
Low plus High RH	476	8 (1.7)	466 (97.9)	2 (0.4)	0.47 (0.20,1.13)	0.090	--	0.999[c]

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormal high platelet count.
--: Results not presented because of the sparse number of participants with an abnormal high platelet count.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-12. Analysis of Platelet Count (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
		Abnormal Low vs. Normal		Abnormal High vs. Normal	
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,204				
Background RH	378	1.40 (0.73,2.70)	0.310	0.86 (0.16,4.61)	0.858
Low RH	237	0.79 (0.33,1.92)	0.604	--	--
High RH	238	0.26 (0.06,1.11)	0.068	3.37 (0.50,22.63)	0.211
Low plus High RH	475	0.45 (0.19,1.09)	0.078	--	--

[a] Relative risk and confidence interval relative to Comparisons.
--: Results not presented because of the sparse number of participants with an abnormal high platelet count.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.
Comparison: 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

(g) MODEL 4: RANCH HANDS — 1987 DIOXIN — UNADJUSTED								
1987 Dioxin Category Summary Statistics					Analysis Results for Log_2 (1987 Dioxin + 1)			
		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
1987 Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[a]	p-Value	Est. Relative Risk (95% C.I.)[a]	p-Value
Low	288	10 (3.5)	276 (95.8)	2 (0.7)	0.70 (0.50,0.96)	0.028	0.95 (0.48,1.88)	0.879
Medium	284	8 (2.8)	276 (97.2)	0 (0.0)				
High	283	4 (1.4)	277 (97.9)	2 (0.7)				

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 15-12. Analysis of Platelet Count (Discrete) (Continued)

(h) MODEL 4: RANCH HANDS — 1987 DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (1987 Dioxin + 1)			
	Abnormal Low vs. Normal		Abnormal High vs. Normal	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
853	0.73 (0.49,1.10)	0.135	0.84 (0.43,1.64)	0.619

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race because of the sparse number of participants with an abnormal high platelet count.

15.2.2.1.11 Prothrombin Time (Continuous)

All results from analyses of prothrombin time in its continuous form were nonsignificant for Models 1 through 4 (Table 15-13: $p \geq 0.22$ for all analyses).

Table 15-13. Analysis of Prothrombin Time (seconds) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***688***	***10.48***	***–0.01 --***	***0.870***
	Comparison	***1,016***	***10.49***		
Officer	Ranch Hand	265	10.54	0.02 --	0.720
	Comparison	402	10.52		
Enlisted Flyer	Ranch Hand	114	10.46	–0.03 --	0.748
	Comparison	157	10.49		
Enlisted Groundcrew	Ranch Hand	309	10.45	–0.02 --	0.714
	Comparison	457	10.47		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***687***	***10.49***	***–0.01 --***	***0.873***
	Comparison	***1,015***	***10.50***		
Officer	Ranch Hand	265	10.52	0.02 --	0.765
	Comparison	402	10.50		
Enlisted Flyer	Ranch Hand	114	10.45	–0.03 --	0.718
	Comparison	157	10.48		
Enlisted Groundcrew	Ranch Hand	308	10.50	–0.02 --	0.762
	Comparison	456	10.51		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 15-13. Analysis of Prothrombin Time (seconds) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	119	10.47	10.48	0.004	–0.001 (0.003)	0.572
Medium	128	10.46	10.46			
High	128	10.45	10.44			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of prothrombin time versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	119	10.48	0.036	0.000 (0.003)	0.956
Medium	128	10.50			
High	128	10.51			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of prothrombin time versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	987	10.49	10.49		
Background RH	309	10.52	10.53	0.04 --	0.476
Low RH	182	10.47	10.46	–0.03 --	0.667
High RH	193	10.45	10.44	–0.05 --	0.411
Low plus High RH	375	10.46	10.45	–0.04 --	0.409

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-13. Analysis of Prothrombin Time (seconds) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	986	10.50		
Background RH	308	10.52	0.02 --	0.695
Low RH	182	10.46	–0.04 --	0.521
High RH	193	10.49	–0.01 --	0.823
Low plus High RH	375	10.47	–0.03 --	0.575

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	235	10.51	0.002	–0.002 (0.002)	0.220
Medium	218	10.50			
High	231	10.45			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of prothrombin time versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	234	10.50	0.016	–0.001 (0.002)	0.685
Medium	218	10.50			
High	231	10.50			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of prothrombin time versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

15.2.2.1.12 Prothrombin Time (Discrete)

All results from analyses of prothrombin time in its discrete form were nonsignificant for Models 1 through 4 (Table 15-14: p>0.29 for all analyses).

Table 15-14. Analysis of Prothrombin Time (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***688***	***10 (1.5)***	***1.14 (0.50,2.61)***	***0.761***
	Comparison	***1,016***	***13 (1.3)***		
Officer	Ranch Hand	265	6 (2.3)	1.31 (0.43,3.93)	0.634
	Comparison	402	7 (1.7)		
Enlisted Flyer	Ranch Hand	114	0 (0.0)	--	0.999[a]
	Comparison	157	1 (0.6)		
Enlisted Groundcrew	Ranch Hand	309	4 (1.3)	1.19 (0.32,4.45)	0.801
	Comparison	457	5 (1.1)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a high prothrombin time.

--: Results not presented because of the sparse number of participants with a high prothrombin time.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.13 (0.49,2.60)***	***0.781***
Officer	1.29 (0.43,3.91)	0.650
Enlisted Flyer	--	--
Enlisted Groundcrew	1.15 (0.30,4.35)	0.838

--: Results not presented because of the sparse number of participants with a high prothrombin time.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	119	2 (1.7)	0.66 (0.28,1.58)	0.315
Medium	128	1 (0.8)		
High	128	1 (0.8)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 15-14. Analysis of Prothrombin Time (Discrete) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
n	Analysis Results for Log_2 (Initial Dioxin) Adjusted Relative Risk (95% C.I.)[a]	p-Value
375	0.72 (0.28,1.85)	0.470

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for occupation and current cigarette smoking because of the sparse number of participants with a high prothrombin time.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	987	13 (1.3)		
Background RH	309	6 (1.9)	1.64 (0.61,4.37)	0.327
Low RH	182	3 (1.7)	1.17 (0.33,4.19)	0.807
High RH	193	1 (0.5)	0.34 (0.04,2.62)	0.297
Low plus High RH	375	4 (1.1)	0.62 (0.17,2.23)	0.461

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	986		
Background RH	308	1.41 (0.52,3.85)	0.501
Low RH	182	1.01 (0.28,3.71)	0.984
High RH	193	0.49 (0.06,3.96)	0.502
Low plus High RH	375	0.70 (0.19,2.57)	0.586

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-14. Analysis of Prothrombin Time (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	235	3 (1.3)	0.86 (0.55,1.34)	0.498
Medium	218	6 (2.8)		
High	231	1 (0.4)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
683	0.86 (0.54, 1.38)	0.526

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for occupation because of the sparse number of participants with a high prothrombin time.

15.2.2.1.13 RBC Morphology

The Model 3 unadjusted analysis revealed a marginally significant difference in RBC morphology between Ranch Hands in the low dioxin category and Comparisons (Table 15-15(e): p=0.051, Est. RR=1.63). After adjustment for covariates, the result was nonsignificant (Table 15-15(f): p=0.206). All results from other analyses of RBC morphology also were nonsignificant (Table 15-15(a–h): p>0.19 for all other analyses).

Table 15-15. Analysis of RBC Morphology

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***64 (7.4)***	***1.18 (0.84,1.66)***	***0.339***
	Comparison	***1,249***	***79 (6.3)***		
Officer	Ranch Hand	341	20 (5.9)	1.03 (0.57,1.87)	0.910
	Comparison	493	28 (5.7)		
Enlisted Flyer	Ranch Hand	151	15 (9.9)	1.10 (0.53,2.29)	0.793
	Comparison	187	17 (9.1)		
Enlisted Groundcrew	Ranch Hand	374	29 (7.8)	1.32 (0.79,2.21)	0.286
	Comparison	569	34 (6.0)		

Table 15-15. Analysis of RBC Morphology (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.16 (0.82,1.64)***	***0.400***
Officer	1.03 (0.57,1.87)	0.923
Enlisted Flyer	1.09 (0.52,2.30)	0.814
Enlisted Groundcrew	1.31 (0.78,2.22)	0.307

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	14 (8.8)	0.94 (0.73,1.21)	0.622
Medium	162	16 (9.9)		
High	156	9 (5.8)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
477	1.02 (0.76,1.38)	0.878

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	73 (6.0)		
Background RH	381	24 (6.3)	1.12 (0.69,1.81)	0.639
Low RH	239	23 (9.6)	1.63 (1.00,2.67)	0.051
High RH	239	16 (6.7)	1.05 (0.60,1.85)	0.862
Low plus High RH	478	39 (8.2)	1.31 (0.87,1.98)	0.196

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-15. Analysis of RBC Morphology (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,210		
Background RH	380	1.18 (0.72,1.93)	0.517
Low RH	238	1.39 (0.84,2.30)	0.206
High RH	239	1.08 (0.60,1.94)	0.800
Low plus High RH	477	1.22 (0.80,1.86)	0.352

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	20 (6.9)	1.03 (0.87,1.23)	0.698
Medium	287	25 (8.7)		
High	284	18 (6.3)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
857	1.02 (0.84,1.25)	0.822

[a] Relative risk for a twofold increase in 1987 dioxin.

15.2.2.1.14 Absolute Neutrophils (Segs)

All Model 1 and 2 results from the analyses of absolute neutrophils (segs) were nonsignificant (Table 15-16(a–d): p>0.11 for each analysis).

Table 15-16. Analysis of Absolute Neutrophils (segs) (thousand/mm³)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***866***	***3.84***	***0.03 --***	***0.612***
	Comparison	***1,249***	***3.81***		
Officer	Ranch Hand	341	3.59	–0.02 --	0.804
	Comparison	493	3.61		
Enlisted Flyer	Ranch Hand	151	3.92	–0.02 --	0.885
	Comparison	187	3.95		
Enlisted Groundcrew	Ranch Hand	374	4.06	0.10 --	0.263
	Comparison	569	3.95		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***864***	***3.46***	***0.01 --***	***0.774***
	Comparison	***1,248***	***3.45***		
Officer	Ranch Hand	340	3.26	–0.02 --	0.808
	Comparison	493	3.28		
Enlisted Flyer	Ranch Hand	151	3.44	–0.03 --	0.804
	Comparison	187	3.47		
Enlisted Groundcrew	Ranch Hand	373	3.68	0.06 --	0.416
	Comparison	568	3.61		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	160	3.77	3.78	0.015	0.019 (0.012)	0.115
Medium	162	4.00	4.00			
High	156	4.02	4.00			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of absolute neutrophils (segs) versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 15-16. Analysis of Absolute Neutrophils (segs) (thousand/mm^3) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	159	3.37	0.198	0.000 (0.012)	0.988
Medium	162	3.43			
High	156	3.38			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute neutrophils (segs) versus log$_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,211	3.82	3.81		
Background RH	381	3.73	3.75	–0.06 --	0.430
Low RH	239	3.81	3.80	–0.01 --	0.906
High RH	239	4.05	4.03	0.22 --	0.028
Low plus High RH	478	3.93	3.91	0.10 --	0.172

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-16. Analysis of Absolute Neutrophils (segs) (thousand/mm^3) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	**n**	**Adj. Mean[a]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]**	**p-Value[c]**
Comparison	1,210	3.45		
Background RH	380	3.45	0.00 --	0.961
Low RH	238	3.44	–0.01 --	0.854
High RH	239	3.50	0.05 --	0.551
Low plus High RH	477	3.47	0.02 --	0.780

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin +1)[b]**		
1987 Dioxin	**n**	**Mean[a]**	**R^2**	**Adjusted Slope (Std. Error)[b]**	**p-Value**
Low	288	3.70	0.007	0.020 (0.008)	0.017
Medium	287	3.79			
High	284	4.04			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute neutrophils (segs) versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**		
1987 Dioxin	**n**	**Adj. Mean[a]**	**R^2**	**Adjusted Slope (Std. Error)[b]**	**p-Value**
Low	287	3.39	0.196	0.006 (0.008)	0.455
Medium	286	3.42			
High	284	3.50			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute neutrophils (segs) versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

The Model 3 unadjusted analysis revealed a significantly higher absolute neutrophil mean for Ranch Hands in the high dioxin category than for Comparisons (Table 15-16(e): p=0.028, difference of adjusted means=0.22 thousand/mm^3). After adjustment for covariates, the difference was nonsignificant (Table 15-16(f): p=0.551). All other Model 3 analyses also were nonsignificant (Table 15-16(e,f): p>0.17 for remaining Model 3 analyses).

A significant positive association between 1987 dioxin levels and absolute neutrophils was revealed from the Model 4 unadjusted analysis (Table 15-16(g): p=0.017, slope=0.020). The association became nonsignificant after adjustment for covariate effects (Table 15-16(h): p=0.455).

15.2.2.1.15 Absolute Neutrophils (Bands) (Nonzero Measurements)

For participants who had a positive number of absolute neutrophils (bands), the unadjusted and adjusted Model 1 analyses revealed a marginally significant difference in absolute neutrophil means between Ranch Hand and Comparison enlisted groundcrew (Table 15-17(a,b): difference of means=0.021 thousand/mm^3, p=0.089; difference of adjusted means=0.016 thousand/mm^3, p=0.099, respectively). The Ranch Hand absolute neutrophil mean was greater than the Comparison mean. All other Model 1 contrasts were nonsignificant (Table 15-17(a,b): p>0.12 for each remaining contrast).

Table 15-17. Analysis of Absolute Neutrophils (bands) (thousand/mm^3) (Nonzero Measurements)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***720***	***0.201***	***0.012 --***	***0.123***
	Comparison	***1,037***	***0.189***		
Officer	Ranch Hand	294	0.194	0.014 --	0.250
	Comparison	406	0.180		
Enlisted Flyer	Ranch Hand	115	0.190	–0.014 --	0.478
	Comparison	160	0.204		
Enlisted Groundcrew	Ranch Hand	311	0.213	0.021 --	0.089
	Comparison	471	0.193		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 15-17. Analysis of Absolute Neutrophils (bands) (thousand/mm^3) (Nonzero Measurements) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***718***	***0.159***	***0.009 --***	***0.126***
	Comparison	***1,036***	***0.150***		
Officer	Ranch Hand	293	0.152	0.011 --	0.221
	Comparison	406	0.141		
Enlisted Flyer	Ranch Hand	115	0.143	–0.013 --	0.389
	Comparison	160	0.156		
Enlisted Groundcrew	Ranch Hand	310	0.177	0.016 --	0.099
	Comparison	470	0.161		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	131	0.194	0.195	0.004	–0.031 (0.032)	0.343
Medium	132	0.249	0.250			
High	134	0.195	0.194			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of absolute neutrophils (bands) versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	130	0.146	0.117	–0.075 (0.036)	0.040
Medium	132	0.174			
High	134	0.132			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute neutrophils (bands) versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 15-17. Analysis of Absolute Neutrophils (bands) (thousand/mm^3) (Nonzero Measurements) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,002	0.189	0.189		
Background RH	316	0.189	0.191	0.002 --	0.783
Low RH	196	0.212	0.211	0.022 --	0.079
High RH	201	0.211	0.209	0.020 --	0.113
Low plus High RH	397	0.211	0.210	0.021 --	0.029

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,001	0.148		
Background RH	315	0.150	0.002 --	0.750
Low RH	195	0.165	0.017 --	0.076
High RH	201	0.161	0.013 --	0.166
Low plus High RH	396	0.163	0.015 --	0.038

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-17. Analysis of Absolute Neutrophils (bands) (thousand/mm³) (Nonzero Measurements) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin +1)[b]**		
1987 Dioxin	**n**	**Mean[a]**	**R^2**	**Slope (Std. Error)[b]**	**p-Value**
Low	241	0.184	0.001	0.015 (0.021)	0.482
Medium	233	0.204			
High	239	0.217			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute neutrophils (bands) versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**		
1987 Dioxin	**n**	**Adj. Mean[a]**	**R^2**	**Adjusted Slope (Std. Error)[b]**	**p-Value**
Low	240	0.136	0.076	0.011 (0.024)	0.657
Medium	232	0.154			
High	239	0.164			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute neutrophils (bands) versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

A significant negative association between initial dioxin and absolute neutrophils (bands) was found in the Model 2 adjusted analysis (Table 15-17(d): p=0.040, adjusted slope=–0.075). Results were nonsignificant in the unadjusted analysis (Table 15-17(c): p=0.343).

The Model 3 contrast of Ranch Hands in the low dioxin category with Comparisons revealed a marginally significant difference of means, indicating a higher absolute neutrophil mean among Ranch Hands than Comparisons (Table 15(e,f): difference of adjusted means=0.022 thousand/mm³, p=0.079; difference of adjusted means=0.017 thousand/mm³, p=0.076, for the unadjusted and adjusted analyses, respectively). Similarly, the mean difference between Ranch Hands in the low and high dioxin categories combined and Comparisons was significant (Table 15-17(e,f): p=0.029, difference of adjusted means=0.021 thousand/mm³; p=0.038, difference of adjusted means=0.015 thousand/mm³, for the unadjusted and adjusted analyses, respectively). All other Model 3 contrasts and each analysis performed from Model 4 were nonsignificant (Table 15-17(e-h): p>0.11 for each remaining contrast).

15.2.2.1.16 Absolute Neutrophils (Bands) (Zero versus Nonzero)

Unadjusted and adjusted Model 1 analyses of the percentage of participants with no absolute neutrophils revealed a significant difference between Ranch Hand and Comparison enlisted flyers (Table 15-18(a,b): p=0.029, Est. RR=1.86; p=0.026, Adj. RR=1.88, for the unadjusted and adjusted analyses, respectively). A greater percentage of Ranch Hand than Comparison enlisted flyers had no absolute neutrophils (23.8% vs. 14.4%). All other Model 1 results and all results from the analyses of Models 2 through 4 were nonsignificant (Table 15-18(a–h): p>0.13 for all remaining analyses).

Table 15-18. Analysis of Absolute Neutrophils (bands) (Zero vs. Nonzero)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Zero	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***146 (16.9)***	***0.99 (0.79,1.25)***	***0.945***
	Comparison	***1,249***	***212 (17.0)***		
Officer	Ranch Hand	341	47 (13.8)	0.75 (0.51,1.10)	0.136
	Comparison	493	87 (17.7)		
Enlisted Flyer	Ranch Hand	151	36 (23.8)	1.86 (1.07,3.23)	0.029
	Comparison	187	27 (14.4)		
Enlisted Groundcrew	Ranch Hand	374	63 (16.8)	0.97 (0.69,1.38)	0.880
	Comparison	569	98 (17.2)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.99 (0.79,1.25)***	***0.956***
Officer	0.74 (0.51,1.09)	0.134
Enlisted Flyer	1.88 (1.08,3.27)	0.026
Enlisted Groundcrew	0.98 (0.69,1.39)	0.918

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Zero	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	29 (18.1)	0.92 (0.76,1.11)	0.381
Medium	162	30 (18.5)		
High	156	22 (14.1)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
477	0.87 (0.70,1.09)	0.214

[a] Relative risk for a twofold increase in initial dioxin.

Table 15-18. Analysis of Absolute Neutrophils (bands) (Zero vs. Nonzero) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	**n**	**Number (%) Zero**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,211	209 (17.3)		
Background RH	381	65 (17.1)	0.98 (0.72,1.34)	0.908
Low RH	239	43 (18.0)	1.05 (0.73,1.51)	0.781
High RH	239	38 (15.9)	0.91 (0.62,1.33)	0.625
Low plus High RH	478	81 (17.0)	0.98 (0.74,1.30)	0.881

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Comparison	1,210		
Background RH	380	1.02 (0.75,1.40)	0.897
Low RH	238	1.03 (0.72,1.49)	0.859
High RH	239	0.88 (0.59,1.30)	0.515
Low plus High RH	477	0.95 (0.72,1.27)	0.741

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**	
1987 Dioxin	**n**	**Number (%) Zero**	**Estimated Relative Risk (95% C.I.)[a]**	**p-Value**
Low	288	47 (16.3)	0.99 (0.88,1.12)	0.905
Medium	287	54 (18.8)		
High	284	45 (15.9)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 15-18. Analysis of Absolute Neutrophils (bands) (Zero vs. Nonzero) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
857	0.92 (0.80,1.06)	0.264

[a] Relative risk for a twofold increase in 1987 dioxin.

15.2.2.1.17 Absolute Lymphocytes

The unadjusted and adjusted Model 2 analyses of absolute lymphocytes revealed a marginally significant positive association between absolute lymphocytes and initial dioxin (Table 15-19(c,d): p=0.063, slope=0.023; p=0.087, adjusted slope=0.024, for the unadjusted and adjusted analyses, respectively). Both analyses showed an increase in absolute lymphocyte levels for increasing initial dioxin levels. Results from each of the analyses of Models 1, 3, and 4 were nonsignificant (Table 15-19(a,b, and e–h): p>0.23 for all analyses).

Table 15-19. Analysis of Absolute Lymphocytes (thousand/mm^3)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***866***	***1.76***	***0.00 --***	***0.920***
	Comparison	***1,249***	***1.75***		
Officer	Ranch Hand	341	1.70	0.04 --	0.392
	Comparison	493	1.67		
Enlisted Flyer	Ranch Hand	151	1.71	–0.08 --	0.248
	Comparison	187	1.79		
Enlisted Groundcrew	Ranch Hand	374	1.83	0.01 --	0.891
	Comparison	569	1.82		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 15-19. Analysis of Absolute Lymphocytes (thousand/mm³) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***864***	***1.79***	***0.00 --***	***0.964***
	Comparison	***1,248***	***1.79***		
Officer	Ranch Hand	340	1.80	0.05 --	0.259
	Comparison	493	1.75		
Enlisted Flyer	Ranch Hand	151	1.74	–0.08 --	0.236
	Comparison	187	1.82		
Enlisted Groundcrew	Ranch Hand	373	1.82	–0.01 --	0.781
	Comparison	568	1.83		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	160	1.68	1.69	0.021	0.023 (0.012)	0.063
Medium	162	1.75	1.75			
High	156	1.83	1.82			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of absolute lymphocytes versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	159	1.76	0.064	0.024 (0.014)	0.087
Medium	162	1.81			
High	156	1.88			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute lymphocytes versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 15-19. Analysis of Absolute Lymphocytes (thousand/mm^3) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,211	1.75	1.75		
Background RH	381	1.75	1.77	0.02 --	0.671
Low RH	239	1.72	1.71	–0.04 --	0.383
High RH	239	1.79	1.78	0.03 --	0.575
Low plus High RH	478	1.75	1.74	–0.01 --	0.839

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,210	1.79		
Background RH	380	1.83	0.04 --	0.356
Low RH	238	1.77	–0.02 --	0.572
High RH	239	1.77	–0.02 --	0.572
Low plus High RH	477	1.77	–0.02 --	0.457

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-19. Analysis of Absolute Lymphocytes (thousand/mm^3) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin +1)[b]		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	288	1.71	0.002	0.009 (0.008)	0.239
Medium	287	1.76			
High	284	1.79			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute lymphocytes versus log$_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	287	1.73	0.050	0.007 (0.009)	0.455
Medium	286	1.79			
High	284	1.79			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute lymphocytes versus log$_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

15.2.2.1.18 Absolute Monocytes

The Model 4 unadjusted analysis of absolute monocytes revealed a marginally significant positive association with 1987 dioxin levels (Table 15-20(g): p=0.059, slope=0.007). This association was nonsignificant after adjustment for covariates (Table 15-20(h): p=0.125). All analysis results from Models 1 through 3 also were nonsignificant (Table 15-20(a–f): p>0.10 for all other analyses).

Table 15-20. Analysis of Absolute Monocytes (thousand/mm^3)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***866***	***0.477***	***–0.004 --***	***0.648***
	Comparison	***1,249***	***0.481***		
Officer	Ranch Hand	341	0.463	–0.008 --	0.594
	Comparison	493	0.471		
Enlisted Flyer	Ranch Hand	151	0.470	–0.037 --	0.118
	Comparison	187	0.507		
Enlisted Groundcrew	Ranch Hand	374	0.492	0.011 --	0.455
	Comparison	569	0.482		

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***864***	***0.471***	***–0.006 --***	***0.544***
	Comparison	***1,248***	***0.476***		
Officer	Ranch Hand	340	0.461	–0.007 --	0.620
	Comparison	493	0.468		
Enlisted Flyer	Ranch Hand	151	0.452	–0.037 --	0.106
	Comparison	187	0.490		
Enlisted Groundcrew	Ranch Hand	373	0.489	0.008 --	0.590
	Comparison	568	0.481		

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

Table 15-20. Analysis of Absolute Monocytes (thousand/mm^3) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	160	0.468	0.469	0.003	0.003 (0.006)	0.568
Medium	162	0.528	0.528			
High	156	0.472	0.470			

[a] Transformed from square root scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on square root of absolute monocytes versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	159	0.463	0.041	0.000 (0.006)	0.999
Medium	162	0.508			
High	156	0.446			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of absolute monocytes versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,211	0.480	0.480		
Background RH	381	0.459	0.464	–0.016 --	0.221
Low RH	239	0.470	0.469	–0.011 --	0.480
High RH	239	0.508	0.502	0.022 --	0.136
Low plus High RH	478	0.489	0.486	0.006 --	0.606

[a] Transformed from square root scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[d] P-value is based on difference of means on square root scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-20. Analysis of Absolute Monocytes (thousand/mm³) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,210	0.479		
Background RH	380	0.464	–0.015 --	0.223
Low RH	238	0.464	–0.015 --	0.319
High RH	239	0.499	0.020 --	0.193
Low plus High RH	477	0.482	0.003 --	0.822

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)[b]		
1987 Dioxin	n	Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	288	0.458	0.004	0.007 (0.004)	0.059
Medium	287	0.467			
High	284	0.503			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of absolute monocytes versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	287	0.450	0.032	0.007 (0.004)	0.125
Medium	286	0.458			
High	284	0.493			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of absolute monocytes versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

15.2.2.1.19 Absolute Eosinophils (Nonzero Measurements)

For participants who had a positive number of absolute eosinophils, all analyses in Models 1 through 4 were nonsignificant (Table 15-21(a–h): p>0.10 for all analyses).

Table 15-21. Analysis of Absolute Eosinophils (thousand/mm³) (Nonzero Measurements)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***760***	***0.159***	***–0.002 --***	***0.684***
	Comparison	***1,096***	***0.161***		
Officer	Ranch Hand	305	0.160	0.007 --	0.422
	Comparison	448	0.153		
Enlisted Flyer	Ranch Hand	134	0.162	–0.002 --	0.895
	Comparison	165	0.164		
Enlisted Groundcrew	Ranch Hand	321	0.157	–0.011 --	0.183
	Comparison	483	0.167		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***758***	***0.151***	***–0.003 --***	***0.576***
	Comparison	***1,095***	***0.154***		
Officer	Ranch Hand	304	0.154	0.007 --	0.347
	Comparison	448	0.147		
Enlisted Flyer	Ranch Hand	134	0.150	–0.003 --	0.806
	Comparison	165	0.153		
Enlisted Groundcrew	Ranch Hand	320	0.149	–0.013 --	0.106
	Comparison	482	0.162		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 15-21. Analysis of Absolute Eosinophils (thousand/mm^3) (Nonzero Measurements) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	139	0.155	0.155	0.001	0.005 (0.025)	0.836
Medium	144	0.154	0.154			
High	134	0.157	0.157			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of absolute eosinophils versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	138	0.151	0.009	0.012 (0.029)	0.670
Medium	144	0.150			
High	134	0.155			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute eosinophils versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 15-21. *Analysis of Absolute Eosinophils (thousand/mm^3) (Nonzero Measurements) (Continued)*

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,064	0.161	0.161		
Background RH	337	0.162	0.163	0.002 --	0.805
Low RH	206	0.156	0.155	–0.006 --	0.513
High RH	211	0.155	0.154	–0.007 --	0.434
Low plus High RH	417	0.155	0.155	–0.006 --	0.346

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,063	0.153		
Background RH	336	0.156	0.003 --	0.677
Low RH	205	0.147	–0.006 --	0.447
High RH	211	0.144	–0.009 --	0.229
Low plus High RH	416	0.146	–0.007 --	0.194

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-21. Analysis of Absolute Eosinophils (thousand/mm^3) (Nonzero Measurements) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin +1)[b]		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	256	0.164	0.001	–0.017 (0.017)	0.330
Medium	250	0.156			
High	248	0.155			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute eosinophils versus log$_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	255	0.156	0.028	–0.010 (0.020)	0.608
Medium	249	0.149			
High	248	0.148			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute eosinophils versus log$_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

15.2.2.1.20 Absolute Eosinophils (Zero versus Nonzero)

The percentage of participants with no absolute eosinophils present was not significantly associated with exposure group or dioxin in any of the Model 1 through 4 analyses (Table 15-22(a–h): p>0.37 for all analyses).

Table 15-22. Analysis of Absolute Eosinophils (Zero vs. Nonzero)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Zero	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***106 (12.2)***	***1.00 (0.77,1.30)***	***0.995***
	Comparison	***1,249***	***153 (12.3)***		
Officer	Ranch Hand	341	36 (10.6)	1.18 (0.74,1.86)	0.493
	Comparison	493	45 (9.1)		
Enlisted Flyer	Ranch Hand	151	17 (11.3)	0.95 (0.49,1.86)	0.885
	Comparison	187	22 (11.8)		
Enlisted Groundcrew	Ranch Hand	374	53 (14.2)	0.93 (0.64,1.34)	0.689
	Comparison	569	86 (15.1)		

Table 15-22. Analysis of Absolute Eosinophils (Zero vs. Nonzero) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.01 (0.77,1.31)***	***0.970***
Officer	1.18 (0.74,1.87)	0.489
Enlisted Flyer	0.95 (0.49,1.87)	0.893
Enlisted Groundcrew	0.92 (0.64,1.34)	0.674

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Zero	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	21 (13.1)	0.95 (0.77,1.17)	0.630
Medium	162	18 (11.1)		
High	156	22 (14.1)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
477	0.92 (0.73,1.18)	0.521

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Zero	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	147 (12.1)		
Background RH	381	44 (11.6)	0.96 (0.67,1.38)	0.833
Low RH	239	33 (13.8)	1.15 (0.77,1.73)	0.487
High RH	239	28 (11.7)	0.95 (0.61,1.46)	0.798
Low plus High RH	478	61 (12.8)	1.04 (0.76,1.44)	0.789

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-22. Analysis of Absolute Eosinophils (Zero vs. Nonzero) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Comparison	1,210		
Background RH	380	1.07 (0.74,1.55)	0.705
Low RH	238	1.16 (0.77,1.76)	0.467
High RH	239	0.82 (0.53,1.27)	0.376
Low plus High RH	477	0.98 (0.71,1.35)	0.885

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**	
1987 Dioxin	**n**	**Number (%) Zero**	**Estimated Relative Risk (95% C.I.)[a]**	**p-Value**
Low	288	32 (11.1)	1.05 (0.91,1.20)	0.528
Medium	287	37 (12.9)		
High	284	36 (12.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
857	0.99 (0.84,1.16)	0.894

[a] Relative risk for a twofold increase in 1987 dioxin.

15.2.2.1.21 Absolute Basophils (Nonzero Measurements)

For participants who had a positive number of absolute basophils, no significant relations were observed between basophils and exposure group or dioxin in Model 1 through 4 analyses (Table 15-23(a–h): p>0.18 for each analysis).

Table 15-23. Analysis of Absolute Basophils (thousand/mm³) (Nonzero Measurements)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	**Group**	**n**	**Mean[a]**	**Difference of Means (95% C.I.)[b]**	**p-Value[c]**
All	***Ranch Hand***	***373***	***0.078***	***–0.002 --***	***0.315***
	Comparison	***580***	***0.080***		
Officer	Ranch Hand	149	0.076	–0.001 --	0.838
	Comparison	232	0.077		
Enlisted Flyer	Ranch Hand	75	0.079	–0.003 --	0.577
	Comparison	87	0.082		
Enlisted Groundcrew	Ranch Hand	149	0.079	–0.003 --	0.322
	Comparison	261	0.082		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	**Group**	**n**	**Adjusted Mean[a]**	**Difference of Adj. Means (95% C.I.)[b]**	**p-Value[c]**
All	***Ranch Hand***	***372***	***0.072***	***–0.002 --***	***0.280***
	Comparison	***580***	***0.074***		
Officer	Ranch Hand	148	0.071	–0.001 --	0.669
	Comparison	232	0.073		
Enlisted Flyer	Ranch Hand	75	0.072	–0.002 --	0.682
	Comparison	87	0.074		
Enlisted Groundcrew	Ranch Hand	149	0.073	–0.003 --	0.326
	Comparison	261	0.076		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 15-23. Analysis of Absolute Basophils (thousand/mm^3) (Nonzero Measurements) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	62	0.077	0.078	0.013	0.009 (0.022)	0.685
Medium	58	0.075	0.076			
High	81	0.081	0.080			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of absolute basophils versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	61	0.073	0.082	–0.003 (0.026)	0.917
Medium	58	0.070			
High	81	0.073			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute basophils versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	562	0.080	0.080		
Background RH	168	0.077	0.078	–0.002 --	0.410
Low RH	92	0.076	0.076	–0.004 --	0.222
High RH	109	0.080	0.080	0.000 --	0.930
Low plus High RH	201	0.078	0.078	–0.002 --	0.482

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-23. Analysis of Absolute Basophils (thousand/mm^3) (Nonzero Measurements) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	562	0.075		
Background RH	168	0.074	–0.001 --	0.657
Low RH	91	0.071	–0.004 --	0.183
High RH	109	0.073	–0.002 --	0.563
Low plus High RH	200	0.072	–0.003 --	0.220

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)[b]		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	132	0.076	<0.001	0.006 (0.014)	0.674
Medium	109	0.079			
High	128	0.078			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute basophils versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	132	0.069	0.076	–0.006 (0.016)	0.716
Medium	108	0.072			
High	128	0.067			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute basophils versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

15.2.2.1.22 Absolute Basophils (Zero versus Nonzero)

Unadjusted and adjusted Model 1 analyses of the percentage of participants with no absolute basophils revealed a significant difference between Ranch Hand and Comparison enlisted groundcrew (Table 15-24(a,b): p=0.068, Est. RR=1.28; p=0.065, Adj. RR=1.28, respectively). A greater percentage of

Ranch Hand than Comparison enlisted groundcrew had no absolute basophils. All other Model 1 contrasts were nonsignificant (Table 15-24(a,b): p>0.10 for each remaining contrast).

Table 15-24. Analysis of Absolute Basophils (Zero vs. Nonzero)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Zero	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***493 (56.9)***	***1.15 (0.96,1.36)***	***0.126***
	Comparison	***1,249***	***669 (53.6)***		
Officer	Ranch Hand	341	192 (56.3)	1.15 (0.87,1.51)	0.338
	Comparison	493	261 (52.9)		
Enlisted Flyer	Ranch Hand	151	76 (50.3)	0.88 (0.57,1.35)	0.565
	Comparison	187	100 (53.5)		
Enlisted Groundcrew	Ranch Hand	374	225 (60.2)	1.28 (0.98,1.67)	0.068
	Comparison	569	308 (54.1)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.16 (0.97,1.38)***	***0.106***
Officer	1.16 (0.88,1.53)	0.303
Enlisted Flyer	0.87 (0.57,1.34)	0.529
Enlisted Groundcrew	1.28 (0.98,1.68)	0.065

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Zero	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	98 (61.3)	0.84 (0.73,0.97)	0.015
Medium	162	104 (64.2)		
High	156	75 (48.1)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 15-24. Analysis of Absolute Basophils (Zero vs. Nonzero) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
477	0.81 (0.68,0.95)	0.012

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Zero	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	649 (53.6)		
Background RH	381	213 (55.9)	1.09 (0.86,1.38)	0.459
Low RH	239	147 (61.5)	1.39 (1.04,1.84)	0.025
High RH	239	130 (54.4)	1.04 (0.78,1.37)	0.796
Low plus High RH	478	277 (58.0)	1.20 (0.97,1.49)	0.098

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,210		
Background RH	380	1.11 (0.87,1.41)	0.395
Low RH	238	1.47 (1.10,1.95)	0.009
High RH	239	1.00 (0.75,1.33)	0.979
Low plus High RH	477	1.21 (0.97,1.50)	0.091

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-24. Analysis of Absolute Basophils (Zero vs. Nonzero) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Zero	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	156 (54.2)	0.97 (0.88,1.06)	0.496
Medium	287	178 (62.0)		
High	284	156 (54.9)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
Analysis Results for Log_2 (1987 Dioxin + 1)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
857	0.94 (0.84,1.05)	0.257

[a] Relative risk for a twofold increase in 1987 dioxin.

Model 2 analyses displayed a significant association between initial dioxin and the percentage of participants with no absolute basophils, both with and without adjustment for covariates (Table 15-24(c,d): p=0.015, Est. RR=0.84; p=0.012, Adj. RR=0.81, respectively). As initial dioxin increased, the percentage of participants with no absolute basophils decreased.

A significant difference in the proportion of participants with no absolute basophils was observed between Ranch Hands in the low dioxin category and Comparisons in both Model 3 unadjusted and adjusted analyses (Table 15-24(e,f): p=0.025, Est. RR=1.39; p=0.009, Adj. RR=1.47, respectively). Also, the contrast of Comparisons with Ranch Hands in the low and high dioxin categories combined was marginally significant in both the unadjusted and adjusted analyses (Table 15-24(e,f): p=0.098, Est. RR=1.20; p=0.091, Adj. RR=1.21, respectively). Ranch Hands in these dioxin categories had a higher percentage of participants with no absolute basophils than did Comparisons. All other Model 3 contrasts, as well as the Model 4 analysis results, were nonsignificant (Table 15-24(e–h): p>0.25 for all analyses).

15.2.3 Longitudinal Analysis

Longitudinal analyses were conducted on platelet count to examine whether changes across time differed with respect to group membership (Model 1), initial dioxin (Model 2), and categorized dioxin (Model 3). Model 4 was not examined in longitudinal analyses because 1987 dioxin—the measure of exposure in these models—changes over time and is not available for all participants for 1982 or 1997.

Discrete and continuous analyses were performed for platelet count. The longitudinal analyses for these variables investigated the difference between the 1982 and 1997 examinations. These analyses were used to investigate the temporal effects of dioxin during the 15-year period between 1982 and 1997.

Participants who were abnormal in 1982 were not included in the longitudinal analysis of discrete dependent variables. The purpose of the longitudinal analysis was to examine the effects of dioxin exposure across time. Participants who were abnormal in 1982 were not considered to be at risk for developing the condition because the condition already existed at the time of the first collection of data for the AFHS (1982). Only participants considered normal at the 1982 examination were considered to be at risk for developing the condition; therefore, the rate of abnormalities under this restriction approximates an incidence rate between 1982 and 1997. That is, an incidence rate is a measure of the rate at which people without a condition develop the condition during a specified period of time (41). Summary statistics are provided for reference purposes for the 1985, 1987, and 1992 examinations.

The longitudinal analyses for platelet count in its discrete form examined relative risks at the 1997 examination for participants who were classified as normal at the 1982 examination. The adjusted relative risks estimated from each of the three models were used to investigate the change in the dependent variable over time. All three models were adjusted for age; Models 2 and 3 also were adjusted for the percentage of body fat at the time of the blood measurement of dioxin.

The longitudinal analysis for the platelet count in its continuous form examined the paired difference between the measurements from 1982 and 1997. These paired differences measured the change in platelet count over time. Each of the three models used in the longitudinal analysis was adjusted for age and platelet count as measured in 1982 (see Chapter 7, Statistical Methods). A square root transformation was applied to platelet count for analytic purposes.

15.2.3.1 Laboratory Variable

15.2.3.1.1 Platelet Count (Continuous)

A decrease was seen in both Ranch Hands and Comparison means between the baseline examination and the 1997 follow-up. The largest portion of the decrease was observed between 1992 and 1997. The change in platelet count means between 1982 and 1997 was examined for associations with group status and dioxin. In the Model 1 analysis, the change in platelet count means between 1982 and 1997 was significantly different between Ranch Hand and Comparison officers (Table 15-25(a): $p<0.001$). The difference was marginally significant in Ranch Hand and Comparison enlisted flyers (Table 15-25(a): $p=0.100$). For both occupations, Ranch Hands have decreased more than Comparisons over the 15-year time period. The difference was nonsignificant when Ranch Hands and Comparisons were examined across all occupations. No significant associations were observed between platelet count and dioxin in Model 2 (Table 15-25(b): $p=0.401$). In the Model 3 analysis, there was a marginally significant difference in the change in platelet count means between the background Ranch Hand dioxin category and Comparisons (Table 15-25(c)). The decrease in means between 1982 and 1997 was greater for Ranch Hands in the background dioxin category (66.0 thousand/mm^3) than for Comparisons (58.6 thousand/mm^3).

Table 15-25. Longitudinal Analysis of Platelet Count (thousand/mm^3) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Mean[a]/(n) Examination 1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	***Ranch Hand***	***273.8 (807)***	***267.8 (788)***	***260.7 (779)***	***250.7 (782)***	***207.2 (807)***	***−66.6***	***−7.8***	***0.203***
	Comparison	***261.7 (966)***	***263.7 (946)***	***255.3 (937)***	***244.4 (944)***	***202.9 (966)***	***−58.8***		
Officer	Ranch Hand	262.4 (307)	258.3 (302)	252.0 (298)	239.3 (299)	196.9 (307)	−65.4	−13.5	<0.001
	Comparison	256.9 (376)	262.5 (370)	253.1 (362)	243.3 (370)	205.0 (376)	−51.9		
Enlisted Flyer	Ranch Hand	281.8 (147)	273.6 (144)	265.7 (142)	255.0 (144)	213.3 (147)	−68.5	−4.1	0.100
	Comparison	258.2 (143)	253.4 (142)	242.6 (141)	235.1 (140)	193.7 (143)	−64.4		
Enlisted Groundcrew	Ranch Hand	280.5 (353)	273.8 (342)	266.3 (339)	259.2 (339)	213.7 (353)	−66.7	−4.0	0.462
	Comparison	266.9 (447)	268.3 (434)	261.3 (434)	248.4 (434)	204.2 (447)	−62.7		

[a] Transformed from square root scale.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of square root of platelet count; results adjusted for square root of platelet count in 1982 and age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

Table 15-25. Longitudinal Analysis of Platelet Count (thousand/mm³) (Continuous) (Continued)

(b) MODEL 2: RANCH HANDS – INITIAL DIOXIN							
Initial Dioxin Category Summary Statistics						Analysis Results for Log_2 (Initial Dioxin)[b]	
	Mean[a]/(n) Examination						
Initial Dioxin	1982	1985	1987	1992	1997	Adjusted Slope (Std. Error)	p-Value
Low	266.5 (152)	265.1 (148)	257.6 (150)	247.0 (147)	204.0 (152)	0.039 (0.046)	0.401
Medium	277.4 (159)	268.2 (156)	262.8 (155)	252.9 (155)	208.0 (159)		
High	284.9 (147)	274.8 (144)	268.5 (142)	259.6 (144)	217.6 (147)		

[a] Transformed from square root scale.
[b] Results based on difference between square root of 1997 platelet count and square root of 1982 platelet count versus $\log_2$ (initial dioxin); results adjusted for percent body fat at the date of the blood measurement of dioxin, square root of 1982 platelet count, and age in 1997.

Notes: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

Table 15-25. Longitudinal Analysis of Platelet Count (thousand/mm³) (Continuous) (Continued)

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY								
Dioxin Category	Mean[a]/(n) Examination 1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
Comparison	261.9 (938)	264.0 (921)	255.7 (911)	245.0 (917)	203.3 (938)	−58.6		
Background RH	270.3 (343)	265.2 (335)	257.5 (327)	247.4 (331)	204.3 (343)	−66.0	−7.4	0.071
Low RH	268.0 (228)	264.0 (221)	258.9 (223)	247.3 (220)	204.0 (228)	−64.0	−5.4	0.544
High RH	284.3 (230)	274.5 (227)	266.8 (224)	258.7 (226)	215.5 (230)	−68.8	−10.2	0.965
Low plus High RH	276.1 (458)	269.3 (448)	262.8 (447)	253.1 (446)	209.7 (458)	−66.4	−7.8	0.676

[a] Transformed from square root scale.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of square root of 1997 platelet count; results adjusted for percent body fat at the date of the blood measurement of dioxin, square root of 1982 platelet count, and age in 1997.

Notes: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

15.2.3.1.2 Platelet Count (Discrete)

The longitudinal analysis of 1997 platelet count in its discrete form was conditioned on participants who had a normal platelet count in 1982. In the Model 1 analyses, no significant difference was observed in the percentage of abnormally low platelet counts between Ranch Hands and Comparisons when all occupations were combined (Table 15-26(a1): p=0.681). Ranch Hand officers had a significantly higher percentage of abnormal low measurements than did Comparison officers (Table 15-26(a1): Adj. RR=2.71, p=0.046), and Ranch Hands enlisted flyers had a significantly smaller percentage of abnormal low measurements than did Comparison officers (Table 15-26(a1): Adj. RR=0.09, p=0.023). No significant differences were observed between Ranch Hands and Comparisons in the percentage of abnormally high measurements, although the sparse number of abnormally high measurements in 1997 precluded meaningful statistical analysis by occupation.

Table 15-26. Longitudinal Analysis of Platelet Count (Abnormal Low vs. Normal and Abnormal High vs. Normal)

(a1) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) Abnormal Low/(n) Examination 1982	1985	1987	1992	1997
All	***Ranch Hand***	***2 (0.3)*** ***807***	***1 (0.1)*** ***788***	***0 (0.0)*** ***779***	***3 (0.4)*** ***782***	***21 (2.6)*** ***807***
	Comparison	***7 (0.7)*** ***966***	***2 (0.2)*** ***946***	***3 (0.3)*** ***937***	***6 (0.6)*** ***944***	***30 (3.1)*** ***966***
Officer	Ranch Hand	1 (0.3) 307	1 (0.3) 302	0 (0.0) 298	2 (0.7) 299	14 (4.6) 307
	Comparison	3 (0.8) 376	0 (0.0) 370	0 (0.0) 362	3 (0.8) 370	7 (1.9) 376
Enlisted Flyer	Ranch Hand	0 (0.0) 147	0 (0.0) 144	0 (0.0) 142	0 (0.0) 144	1 (0.7) 147
	Comparison	0 (0.0) 143	1 (0.7) 142	2 (1.4) 141	1 (0.7) 140	10 (7.0) 143
Enlisted Groundcrew	Ranch Hand	1 (0.3) 353	0 (0.0) 342	0 (0.0) 339	1 (0.3) 339	6 (1.7) 353
	Comparison	4 (0.9) 447	1 (0.2) 434	1 (0.2) 434	2 (0.5) 434	13 (2.9) 447

Occupational Category	Group	Normal in 1982: n in 1997	Number (%) Abnormal Low in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***799***	***20 (2.5)***	***0.88 (0.49,1.59)***	***0.681***
	Comparison	***950***	***27 (2.8)***		
Officer	Ranch Hand	305	13 (4.3)	2.71 (1.02,7.23)	0.046
	Comparison	372	6 (1.6)		
Enlisted Flyer	Ranch Hand	146	1 (0.7)	0.09 (0.01,0.71)	0.023
	Comparison	141	10 (7.1)		
Enlisted Groundcrew	Ranch Hand	348	6 (1.7)	0.71 (0.26,1.94)	0.501
	Comparison	437	11 (2.5)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal platelet count in 1982 (see Chapter 7, Statistical Methods).

Table 15-26. Longitudinal Analysis of Platelet Count (Abnormal Low vs. Normal and Abnormal High vs. Normal) (Continued)

(a2) MODEL 1: RANCH HANDS VS. COMPARISONS						
		Number (%) Abnormal High/(n) Examination				
Occupational Category	Group	1982	1985	1987	1992	1997
All	***Ranch Hand***	***6 (0.7)***	***12 (1.5)***	***16 (2.1)***	***9 (1.2)***	***4 (0.5)***
		807	***788***	***779***	***782***	***807***
	Comparison	***9 (0.9)***	***13 (1.4)***	***13 (1.4)***	***8 (0.9)***	***4 (0.4)***
		966	***946***	***937***	***944***	***966***
Officer	Ranch Hand	1 (0.3)	3 (1.0)	4 (1.3)	0 (0.0)	1 (0.3)
		307	302	298	299	307
	Comparison	1 (0.3)	3 (0.8)	5 (1.4)	3 (0.8)	3 (0.8)
		376	370	362	370	376
Enlisted Flyer	Ranch Hand	1 (0.7)	3 (2.1)	4 (2.8)	1 (0.7)	1 (0.7)
		147	144	142	144	147
	Comparison	2 (1.4)	3 (2.1)	1 (0.7)	2 (1.4)	1 (0.7)
		143	142	141	140	143
Enlisted Groundcrew	Ranch Hand	4 (1.1)	6 (1.8)	8 (2.4)	8 (2.4)	2 (0.6)
		353	342	339	339	353
	Comparison	6 (1.3)	7 (1.6)	7 (1.6)	3 (0.7)	0 (0.0)
		447	434	434	434	447

		Normal in 1982			
Occupational Category	Group	n in 1997	Number (%) Abnormal High in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***799***	***3 (0.4)***	***1.81 (0.30,10.89)***	***0.516***
	Comparison	***950***	***2 (0.2)***		
Officer	Ranch Hand	305	1 (0.3)	--	0.999[b]
	Comparison	372	2 (0.5)		
Enlisted Flyer	Ranch Hand	146	1 (0.7)	--	0.999[b]
	Comparison	141	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	348	1 (0.3)	--	0.912[b]
	Comparison	437	0 (0.0)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1997 results; results adjusted for age in 1997.
[b] P-value not presented because of the sparse number of participants with an abnormal high platelet count; results not adjusted for age in 1997.
--: Results not presented because of the sparse number of participants with an abnormal high platelet count.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal platelet count in 1982 (see Chapter 7, Statistical Methods).

Table 15-26. Longitudinal Analysis of Platelet Count (Abnormal Low vs. Normal and Abnormal High vs. Normal) (Continued)

(b1) MODEL 2: RANCH HANDS — INITIAL DIOXIN					
	Number (%) Abnormal Low/(n) Examination				
Initial Dioxin	1982	1985	1987	1992	1997
Low	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	3 (2.0)
	152	148	150	147	152
Medium	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (2.5)
	159	156	155	155	159
High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)
	147	144	142	144	147

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1982			
Initial Dioxin	n in 1997	Number (%) Abnormal Low in 1997	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	150	2 (1.3)	0.83 (0.43,1.61)	0.586
Medium	158	4 (2.5)		
High	146	1 (0.7)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Notes: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal platelet count in 1982 (see Chapter 7, Statistical Methods).

(b2) MODEL 2: RANCH HANDS — INITIAL DIOXIN					
	Number (%) Abnormal High/(n) Examination				
Initial Dioxin	1982	1985	1987	1992	1997
Low	1 (0.7)	1 (0.7)	3 (2.0)	1 (0.7)	0 (0.0)
	152	148	150	147	152
Medium	1 (0.6)	2 (1.3)	4 (2.6)	3 (1.9)	1 (0.6)
	159	156	155	155	159
High	1 (0.7)	3 (2.1)	3 (2.1)	4 (2.8)	1 (0.7)
	147	144	142	144	147

Table 15-26. Longitudinal Analysis of Platelet Count (Abnormal Low vs. Normal and Abnormal High vs. Normal) (Continued)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1982			
Initial Dioxin	n in 1997	Number (%) Abnormal High in 1997	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	150	0 (0.0)	1.28 (0.32,5.19)	0.726
Medium	158	1 (0.6)		
High	146	0 (0.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Notes: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal platelet count in 1982 (see Chapter 7, Statistical Methods).

(c1) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY					
	Number (%) Abnormal Low/(n) Examination				
Dioxin Category	1982	1985	1987	1992	1997
Comparison	6 (0.6) 938	1 (0.1) 921	2 (0.2) 911	4 (0.4) 917	28 (3.0) 938
Background RH	1 (0.3) 343	1 (0.3) 335	0 (0.0) 327	2 (0.6) 331	12 (3.5) 343
Low RH	1 (0.4) 228	0 (0.0) 221	0 (0.0) 223	1 (0.5) 220	6 (2.6) 228
High RH	0 (0.0) 230	0 (0.0) 227	0 (0.0) 224	0 (0.0) 226	2 (0.9) 230
Low plus High RH	1 (0.2) 458	0 (0.0) 448	0 (0.0) 447	1 (0.2) 446	8 (1.8) 458

Table 15-26. Longitudinal Analysis of Platelet Count (Abnormal Low vs. Normal and Abnormal High vs. Normal) (Continued)

Dioxin Category	Normal in 1982 n in 1997	Normal in 1982 Number (%) Abnormal Low in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	923	26 (2.8)		
Background RH	339	12 (3.5)	1.33 (0.66,2.69)	0.424
Low RH	226	5 (2.2)	0.70 (0.26,1.85)	0.471
High RH	228	2 (0.9)	0.32 (0.07,1.36)	0.122
Low plus High RH	454	7 (1.5)	0.47 (0.19,1.18)	0.107

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

Notes: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal platelet count in 1982 (see Chapter 7, Statistical Methods).

(c2) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY

Dioxin Category	Number (%) Abnormal High/(n) Examination 1982	1985	1987	1992	1997
Comparison	9 (1.0) 938	13 (1.4) 921	13 (1.4) 911	8 (0.9) 917	4 (0.4) 938
Background RH	3 (0.9) 343	5 (1.5) 335	6 (1.8) 327	1 (0.3) 331	2 (0.6) 343
Low RH	1 (0.4) 228	2 (0.9) 221	4 (1.8) 223	2 (0.9) 220	0 (0.0) 228
High RH	2 (0.9) 230	4 (1.8) 227	6 (2.7) 224	6 (2.7) 226	2 (0.9) 230
Low plus High RH	3 (0.7) 458	6 (1.3) 448	10 (2.2) 447	8 (1.8) 446	2 (0.4) 458

Table 15-26. Longitudinal Analysis of Platelet Count (Abnormal Low vs. Normal and Abnormal High vs. Normal) (Continued)

	Normal in 1982			
Dioxin Category	n in 1997	Number (%) Abnormal High in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	923	2 (0.2)		
Background RH	339	2 (0.6)	2.17 (0.30,15.65)	0.442
Low RH	226	0 (0.0)	--	0.999[c]
High RH	228	1 (0.4)	3.79 (0.32,45.31)	0.293
Low plus High RH	454	1 (0.2)	--	0.999[c]

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[c] P-value not presented because of the sparse number of participants with an abnormal high platelet count; results not adjusted for age in 1997.
--: Results not presented because of the sparse number of participants with an abnormal high platelet count.

Notes: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal platelet count in 1982 (see Chapter 7, Statistical Methods).

Model 2 analyses did not show a significant association of initial dioxin with either abnormally low or abnormally high platelet counts (Table 15-26(b1) and (b2): p>0.58 for each analysis). The Model 3 analyses of categorized dioxin also did not show any significant associations with abnormal platelet count levels (Table 15-26(c1) and (c2): p>0.10 for all analyses).

15.3 DISCUSSION

As indices of the three peripheral blood lines—RBCs, WBCs, and platelets—the hematologic variables analyzed are widely used in clinical medicine and are relied upon heavily to reflect disease not only of the hematopoietic system, but in other organ systems as well. Although lacking specificity, abnormalities in the hemoglobin, hematocrit, and total WBC count often serve as a sensitive first alert to the presence of a host of infection, inflammatory, and neoplastic disease states across multiple organ systems and point to the need for further investigation.

As elements essential to normal coagulation, the platelets have a short half-life and are most subject to decreased survival in a wide range of diseases, toxic chemical exposures, and in the presence of numerous over-the-counter and prescription medications. The broad range of normal for the platelet count (130 thousand/mm^3 to 400 thousand/mm^3) is such that subtle changes in platelet survival can occur and not be identified as abnormal. Only extreme variations in the platelet count—less than 50 thousand/mm^3 and

greater than 800 thousand/mm^3—are associated with the classic complications of spontaneous bleeding or blood clot formation.

Similar to the 1987 and 1992 examinations, most of the significant results were limited to the platelet and WBC analyses. Ranch Hand enlisted flyers and groundcrew had higher mean platelet counts than Comparisons, but the differences in the means (14.9 thousand/mm^3 and 9.3 thousand/mm^3, respectively) cannot be considered biologically meaningful.

Few of the serum dioxin analyses yielded significant results. In a pattern consistent with a dose-response effect, a positive association was noted between the mean platelet count and initial dioxin levels in the low, medium, and high categories. When adjusted for covariates, the associations were no longer significant. Similarly, in the model using 1987 dioxin levels, Ranch Hands with the highest levels of serum dioxin had significantly higher mean platelet counts than did Comparisons, but after adjustment for covariates, the association was not significant. Once again, the difference in the means was relatively small (never more than 14 thousand/mm^3). In the discrete analyses, which can be considered more relevant clinically, no significant group or occupational differences were noted, nor was there any evidence for a dioxin effect.

In the 1987 examinations, the mean WBC and platelet counts and the erythrocyte sedimentation rates were higher in Ranch Hands than Comparisons, raising the possibility of a subclinical inflammatory response associated with prior dioxin exposure. In the current study as in 1992, no significant group differences were noted in any of these indices. The unadjusted analyses of the WBC and platelet variables and, as noted in Chapter 9, of erythrocyte sedimentation rate, have yielded results consistent with a subtle dose-response effect in relation to both initial and 1987 dioxin levels. After adjustment for covariates, none of the findings remained significant.

Dependent variable-covariate associations confirmed numerous observations that have been well-established in clinical practice. In cigarette smokers, cellular hypoxia related to carboxyhemoglobin formation and systemic arterial desaturation in obstructive airway disease combine to raise the hemoglobin and hematocrit in comparison to nonsmokers. The increased incidence of chronic bronchitis in smokers is often associated with an elevation in the total WBC count. Of participants smoking at least one pack per day, 16.1 percent had abnormally elevated WBC counts, versus a prevalence of 1.4 percent in nonsmokers ($p=0.001$). Older participants were found to have statistically significant reductions in the total RBC, hemoglobin, and hematocrit associations that may reflect the increased incidence of chronic disease associated with age.

Race-related associations were noted. When compared to non-Black participants, Black participants had statistically significant reductions in the RBC indices, findings that may relate to the increased incidence of glucose-6-phosphate dehydrogenase (G-6-PD) deficiency and of hemoglobin variants (S and C) associated with heterozygous sickling disorders. Blacks were found to have a greater prevalence of abnormally low RBC counts than non-Blacks (7.8% vs. 4.6%), although the difference in the means (4.99 thousand/mm^3 vs. 4.95 thousand/mm^3) is not statistically significant and is not likely clinically meaningful.

The longitudinal analyses documented a reduction in the total platelet count in each group and across all occupational strata. As documented in the 1987 follow-up report, Ranch Hands continue to have a greater reduction in the total platelet count over time than do Comparisons, although the current means (207.2 thousand/mm^3 vs. 202.9 thousand/mm^3) are nearly equal.

In conclusion, analyses of 13 hematologic variables yielded no significant group differences between the Ranch Hand and Comparison cohorts, and these results are consistent with the 1992 follow-up examination. In those participants most heavily exposed, the slight increase in the platelet count referenced above may still reflect a subtle biologic effect of dioxin exposure. Apart from platelet count, there appears to be little evidence to support a relation between dioxin exposure and adverse effects to the hematopoietic system.

15.4 SUMMARY

The hematology assessment included analyses of 13 variables each from the laboratory examination. For each variable, associations with group (Model 1), initial dioxin (Model 2), categorized dioxin (Model 3), and 1987 dioxin (Model 4) were assessed. Continuous and discrete analyses were performed for each cell count variable as well as for prothrombin time. RBC morphology, as well as blood count variables, was also analyzed. In addition, due to the large number of nonzero measurements for absolute neutrophils (bands), absolute eosinophils, and absolute basophils, investigations on these variables consisted of two analyses. First, a discrete analysis was performed on the proportion of zero measurements, and second, a continuous analysis was performed on the nonzero measurements.

15.4.1 Model 1: Group Analysis

As shown in Table 15-27, in both the unadjusted and adjusted analyses of the cell count variables, only the analyses of platelet count revealed significant group differences. In the continuous analysis, group differences were significant for each occupation but not significant when examined across all occupations. The platelet count mean was higher for Comparison officers and higher for Ranch Hands in both enlisted flyers and enlisted groundcrew. In the discrete analysis of platelet count, unadjusted and adjusted results also revealed consistent results. Significant group differences in the percentage of abnormally low platelet counts were found within the officer and enlisted flyer strata. For officers, more Ranch Hands than Comparisons exhibited an abnormally low platelet count. Conversely, for enlisted flyers, more Comparisons than Ranch Hands had an abnormally low platelet count.

Table 15-27. Summary of Group Analysis (Model 1) for Hematology Variables (Ranch Hands vs. Comparisons)

	UNADJUSTED			
Variable	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Laboratory				
Red Blood Cell (RBC) Count (C)	ns	ns	ns	NS
Red Blood Cell (RBC) Count (D)				
Abnormal Low vs. Normal	NS	ns	NS	ns
Abnormal High vs. Normal	ns	ns	NS	ns
White Blood Cell (WBC) Count (C)	NS	NS	ns	NS
White Blood Cell (WBC) Count (D)				
Abnormal Low vs. Normal	NS	NS	NS	NS
Abnormal High vs. Normal	NS	ns	NS	NS
Hemoglobin (C)	NS	ns	ns	NS
Hemoglobin (D)				
Abnormal Low vs. Normal	NS	NS	NS	ns
Abnormal High vs. Normal	ns	NS	NS	ns

Table 15-27. Summary of Group Analysis (Model 1) for Hematology Variables (Ranch Hands vs. Comparisons) (Continued)

Variable	UNADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Hematocrit (C)	ns	ns	ns	NS
Hematocrit (D)				
Abnormal Low vs. Normal	NS	ns	NS	ns
Abnormal High vs. Normal	ns	ns	NS	ns
Platelet Count (C)	NS	−0.012	+0.005	+0.004
Platelet Count (D)				
Abnormal Low vs. Normal	ns	+0.021	−0.032	ns
Abnormal High vs. Normal	NS	ns	NS	NS
Prothrombin Time (C)	ns	NS	ns	ns
Prothrombin Time (D)	NS	NS	ns	NS
RBC Morphology (D)	NS	NS	NS	NS
Absolute Neutrophils (Segs) (C)	NS	ns	ns	NS
Absolute Neutrophils (Bands) (Nonzero Measurements) (C)	NS	NS	ns	NS*
Absolute Neutrophils (Bands) (Zero vs. Nonzero) (D)	ns	ns	+0.029	ns
Absolute Lymphocytes (C)	NS	NS	ns	NS
Absolute Monocytes (C)	ns	ns	ns	NS
Absolute Eosinophils (Nonzero Measurements) (C)	ns	NS	ns	ns
Absolute Eosinophils (Zero vs. Nonzero) (D)	NS	NS	ns	ns
Absolute Basophils (Nonzero Measurements) (C)	ns	ns	ns	ns
Absolute Basophils (Zero vs. Nonzero) (D)	NS	NS	ns	NS*

Note: NS*: Marginally significant ($0.05<p\leq 0.10$).
NS or ns: Not significant ($p>0.10$).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00 for discrete analysis; difference of means nonnegative for continuous analysis.
−: Relative risk<1.00 for discrete analysis; difference of means negative for continuous analysis.

P-value given if $p\leq 0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 15-27. Summary of Group Analysis (Model 1) for Hematology Variables (Ranch Hands vs. Comparisons) (Continued)

Variable	ADJUSTED All	Officer	Enlisted Flyer	Enlisted Groundcrew
Laboratory				
Red Blood Cell (RBC) Count (C)	ns	ns	ns	NS
Red Blood Cell (RBC) Count (D)				
Abnormal Low vs. Normal	NS	ns	NS	ns
Abnormal High vs. Normal	ns	ns	NS	ns
White Blood Cell (WBC) Count (C)	NS	NS	ns	NS
White Blood Cell (WBC) Count (D)				
Abnormal Low vs. Normal	NS	NS	NS	NS
Abnormal High vs. Normal	ns	ns	ns	ns
Hemoglobin (C)	ns	ns	ns	NS
Hemoglobin (D)				
Abnormal Low vs. Normal	NS	NS	NS	ns
Abnormal High vs. Normal	ns	NS	--	--
Hematocrit (C)	ns	ns	ns	NS
Hematocrit (D)				
Abnormal Low vs. Normal	NS	ns	NS	ns
Abnormal High vs. Normal	ns	--	--	--
Platelet Count (C)	NS	−0.014	+0.003	+0.011
Platelet Count (D)				
Abnormal Low vs. Normal	ns	+0.022	−0.029	ns
Abnormal High vs. Normal	NS	ns	NS	NS
Prothrombin Time (C)	ns	NS	ns	ns
Prothrombin Time (D)	NS	NS	--	NS
RBC Morphology (D)	NS	NS	NS	NS
Absolute Neutrophils (Segs) (C)	NS	ns	ns	NS
Absolute Neutrophils (Bands) (Nonzero Measurements) (C)	NS	NS	ns	NS*
Absolute Neutrophils (Bands) (Zero vs. Nonzero) (D)	ns	ns	+0.026	ns
Absolute Lymphocytes (C)	NS	NS	ns	ns
Absolute Monocytes (C)	ns	ns	ns	NS
Absolute Eosinophils (Nonzero Measurements) (C)	ns	NS	ns	ns
Absolute Eosinophils (Zero vs. Nonzero) (D)	NS	NS	ns	ns
Absolute Basophils (Nonzero Measurements) (C)	ns	ns	ns	ns
Absolute Basophils (Zero vs. Nonzero) (D)	NS	NS	ns	NS*

Note: NS* or ns*: Marginally significant ($0.05<p\leq0.10$).
NS or ns: Not significant ($p>0.10$).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00 for discrete analysis; difference of means nonnegative for continuous analysis.
−: Relative risk<1.00 for discrete analysis; difference of means negative for continuous analysis.
--: Analysis not performed because of the sparse number of participants with an abnormality.

P-value given if $p\leq0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

The unadjusted and adjusted results from the analyses of the blood count variables also were similar. The continuous analyses of absolute neutrophils (bands) revealed a marginally significant higher mean for Ranch Hands within the enlisted groundcrew stratum. A greater percentage of zero measurements were found among Ranch Hand enlisted flyers than among Comparison enlisted flyers. For the analysis of absolute basophils, the difference in the proportions of zero measurements was marginally significant and higher for Ranch Hands than for Comparisons within the enlisted groundcrew stratum.

15.4.2 Model 2: Initial Dioxin Analysis

Unadjusted analyses of the cell count variables revealed several significant associations with initial dioxin, as shown in Table 15-28. The continuous analyses of WBC count, hemoglobin, hematocrit, and platelet count each showed a significant, positive relation with initial dioxin. After adjustment for covariate information, each association was nonsignificant. Other significant results include the discrete unadjusted and adjusted analyses of WBC count, revealing a decrease in the proportion of abnormally low WBC counts as initial dioxin increased.

Table 15-28. Summary of Initial Dioxin Analysis (Model 2) for Hematology Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Laboratory		
Red Blood Cell (RBC) Count (C)	NS	ns
Red Blood Cell (RBC) Count (D)		
Abnormal Low vs. Normal	ns	ns
Abnormal High vs. Normal	ns	ns
White Blood Cell (WBC) Count (C)	+0.035	NS
White Blood Cell (WBC) Count (D)		
Abnormal Low vs. Normal	−0.012	−0.043
Abnormal High vs. Normal	ns	ns
Hemoglobin (C)	+0.023	NS
Hemoglobin (D)		
Abnormal Low vs. Normal	ns*	ns
Abnormal High vs. Normal	NS	NS
Hematocrit (C)	+0.021	NS
Hematocrit (D)		
Abnormal Low vs. Normal	ns	NS
Abnormal High vs. Normal	NS	NS
Platelet Count (C)	+0.012	NS
Platelet Count (D)		
Abnormal Low vs. Normal	ns	ns
Abnormal High vs. Normal	NS	ns
Prothrombin Time (C)	ns	NS
Prothrombin Time (D)	ns	ns
RBC Morphology	ns	NS
Absolute Neutrophils (Segs) (C)	NS	NS
Absolute Neutrophils (Bands) (Nonzero Measurements) (C)	ns	−0.040
Absolute Neutrophils (Bands) (Zero vs. Nonzero) (D)	ns	ns

Table 15-28. Summary of Initial Dioxin Analysis (Model 2) for Hematology Variables (Ranch Hands Only) (Continued)

Variable	Unadjusted	Adjusted
Absolute Lymphocytes (C)	NS*	NS*
Absolute Monocytes (C)	NS	NS
Absolute Eosinophils (Nonzero Measurements) (C)	NS	NS
Absolute Eosinophils (Zero vs. Nonzero) (D)	ns	ns
Absolute Basophils (Nonzero Measurements) (C)	NS	ns
Absolute Basophils (Zero vs. Nonzero) (D)	−0.015	−0.012

Note: NS or ns: Not significant (p>0.10).
NS* or ns*: Marginally significant (0.05<p≤0.10).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00 for discrete analysis.
−: Relative risk<1.00; slope negative for continuous analysis.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or slope nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

Among the blood count variables, the result from the unadjusted analysis of absolute neutrophils (bands) was nonsignificant. After adjustment for covariates, a significant negative association was revealed, where neutrophils decreased as initial dioxin increased. A marginally significant and positive association between initial dioxin and absolute lymphocyte count was found in both the unadjusted and adjusted analyses. In addition, a significant negative association between initial dioxin and the proportion of zero measurements was revealed in both the unadjusted and adjusted analyses of absolute basophils.

15.4.3 Model 3: Categorized Dioxin Analysis

Several contrasts that were marginally significant or significant in the unadjusted categorized dioxin analyses of the cell count variables and RBC morphology became nonsignificant or marginally significant in the adjusted analyses. A summary of the results of the categorized dioxin analysis is provided in Table 15-29. The contrast of Ranch Hands in the low dioxin category with Comparisons for RBC count was marginally significant without adjustment for covariates but nonsignificant after adjustment. When Ranch Hands in the high dioxin category were contrasted with Comparisons in the unadjusted, continuous analysis of WBC count, a significant difference was revealed. In the adjusted analysis the result was nonsignificant. The unadjusted contrast of Ranch Hands in the low dioxin category, with Comparisons in the discrete analysis of WBC count resulted in a significant difference, although the difference was marginally significant in the adjusted analysis. Continuous hemoglobin analysis revealed a marginally significant difference between Ranch Hands in the high category and Comparisons. In addition, analysis of RBC morphology revealed a marginally significant difference between Ranch Hands in the low dioxin category and Comparisons. After adjustment for covariates for both hemoglobin and RBC morphology, the results were nonsignificant. Except for the low Ranch Hand contrast for RBC count, each of the aforementioned contrasts displayed either a greater percentage of Ranch Hands with an abnormality or Ranch Hands with a higher cell count mean.

Table 15-29. Summary of Categorized Dioxin Analysis (Model 3) for Hematology Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Laboratory				
Red Blood Cell (RBC) Count (C)	ns	ns*	NS	ns
Red Blood Cell (RBC) Count (D)				
Abnormal Low vs. Normal	NS	NS	ns	ns
Abnormal High vs. Normal	ns	ns	ns	ns
White Blood Cell (WBC) Count (C)	ns	ns	+0.029	NS
White Blood Cell (WBC) Count (D)				
Abnormal Low vs. Normal	NS	+0.027	ns	NS
Abnormal High vs. Normal	ns	ns	NS	NS
Hemoglobin (C)	ns	ns	NS*	NS
Hemoglobin (D)				
Abnormal Low vs. Normal	NS	NS	ns	ns
Abnormal High vs. Normal	NS	ns	ns	ns
Hematocrit (C)	ns	ns	NS	NS
Hematocrit (D)				
Abnormal Low vs. Normal	ns	ns	ns	ns
Abnormal High vs. Normal	ns	ns	ns	ns
Platelet Count (C)	ns	ns	+<0.001	+0.017
Platelet Count (D)				
Abnormal Low vs. Normal	NS	ns	ns*	ns*
Abnormal High vs. Normal	NS	ns	NS	ns
Prothrombin Time (C)	NS	ns	ns	ns
Prothrombin Time (D)	NS	NS	ns	ns
RBC Morphology	NS	NS*	NS	NS
Absolute Neutrophils (Segs) (C)	ns	ns	+0.028	NS
Absolute Neutrophils (Bands) (Nonzero Measurements) (C)	NS	NS*	NS	+0.029
Absolute Neutrophils (Bands) (Zero vs. Nonzero) (D)	ns	NS	ns	ns
Absolute Lymphocytes (C)	NS	ns	NS	ns
Absolute Monocytes (C)	ns	ns	NS	NS
Absolute Eosinophils (Nonzero Measurements) (C)	NS	ns	ns	ns
Absolute Eosinophils (Zero vs. Nonzero) (D)	ns	NS	ns	NS
Absolute Basophils (Nonzero Measurements) (C)	ns	ns	NS	ns
Absolute Basophils (Zero vs. Nonzero) (D)	NS	+0.025	NS	NS*

Table 15-29. Summary of Categorized Dioxin Analysis (Model 3) for Hematology Variables (Ranch Hands vs. Comparisons) (Continued)

Note: NS or ns: Not significant (p>0.10).
NS* or ns*: Marginally significant (0.05<p≤0.10).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00 for discrete analysis; difference of means nonnegative for continuous analysis.
--: Analysis not performed because of the sparse number of participants with an abnormality.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Variable	ADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Laboratory				
Red Blood Cell (RBC) Count (C)	NS	ns	ns	ns
Red Blood Cell (RBC) Count (D)				
Abnormal Low vs. Normal	NS	ns	NS	ns
Abnormal High vs. Normal	ns	ns	NS	ns
White Blood Cell (WBC) Count (C)	NS	ns	NS	ns
White Blood Cell (WBC) Count (D)				
Abnormal Low vs. Normal	NS	NS*	ns	NS
Abnormal High vs. Normal	ns	ns	NS	ns
Hemoglobin (C)	ns	ns	NS	NS
Hemoglobin (D)				
Abnormal Low vs. Normal	NS	ns	ns	ns
Abnormal High vs. Normal	NS	--	ns	--
Hematocrit (C)	ns	ns	NS	ns
Hematocrit (D)				
Abnormal Low vs. Normal	NS	ns	NS	ns
Abnormal High vs. Normal	--	--	ns	--
Platelet Count (C)	ns	NS	+0.002	+0.038
Platelet Count (D)				
Abnormal Low vs. Normal	NS	ns	ns*	ns*
Abnormal High vs. Normal	ns	--	NS	--
Prothrombin Time (C)	NS	ns	ns	ns
Prothrombin Time (D)	NS	NS	ns	ns
RBC Morphology	NS	NS	NS	NS
Absolute Neutrophils (Segs) (C)	NS	ns	NS	NS
Absolute Neutrophils (Bands) (Nonzero Measurements) (C)	NS	NS*	NS	+0.038
Absolute Neutrophils (Bands) (Zero vs. Nonzero) (D)	NS	NS	ns	ns
Absolute Lymphocytes (C)	NS	ns	ns	ns
Absolute Monocytes (C)	ns	ns	NS	NS

Table 15-29. Summary of Categorized Dioxin Analysis (Model 3) for Hematology Variables (Ranch Hands vs. Comparisons) (Continued)

	ADJUSTED			
Variable	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Absolute Eosinophils (Nonzero Measurements) (C)	NS	ns	ns	ns
Absolute Eosinophils (Zero vs. Nonzero) (D)	NS	NS	ns	ns
Absolute Basophils (Nonzero Measurements) (C)	ns	ns	ns	ns
Absolute Basophils (Zero vs. Nonzero) (D)	NS	+0.009	NS	NS*

Note: NS or ns: Not significant ($p>0.10$).
NS* or ns*: Marginally significant ($0.05<p\leq0.10$).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00 for discrete analysis; difference of means nonnegative for continuous analysis.
--: Analysis not performed because of the sparse number of participants with an abnormality.

P-value given if $p\leq0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Results from the analyses of platelet count, both in the continuous and discrete forms, were consistent in the unadjusted and adjusted analyses. Significantly higher mean platelet counts were observed for Ranch Hands in the high and in the low and high dioxin categories combined than for Comparisons. The discrete analysis of platelet count revealed a marginally significant lower percentage of abnormally low platelet counts for Ranch Hands in the high and in the low and high dioxin categories combined than for Comparisons.

The analysis of the blood count variables revealed significant results for absolute neutrophils (segs) and absolute neutrophils (bands) in the continuous form and absolute basophils (zero versus nonzero measurements). A significant difference between Ranch Hands in the high dioxin category and Comparisons was found in the unadjusted analysis of absolute neutrophils (segs). The result was nonsignificant in the adjusted analysis. In both the unadjusted and adjusted analyses of absolute neutrophils (bands) in the continuous form, a marginally significant difference of means was found among Ranch Hands in the low dioxin category and Comparisons. Also, a significant absolute neutrophil (bands) mean difference was found among Ranch Hands in the low and high dioxin categories combined and Comparisons for both the unadjusted and adjusted analyses. Results were consistent in the unadjusted and adjusted analyses of absolute basophils (zero versus nonzero measurements). A significant difference in the proportion of zero absolute basophil measurements was found among Ranch Hands in the low dioxin category and Comparisons. A marginally significant difference was found when contrasting the low and high Ranch Hand dioxin categories with Comparisons. Both results indicate that more Ranch Hands than Comparisons had a zero absolute basophil measurement.

15.4.4 Model 4: 1987 Dioxin

In the unadjusted analyses, several significant and marginally significant results were found. The results are summarized in Table 15-30. Except for the analysis of the discrete form of WBC, each result became nonsignificant in the adjusted analysis. The significant association between continuous WBC count and 1987 dioxin was positive, as were the associations with continuous platelet count and absolute neutrophils (segs). Significant negative associations between 1987 dioxin and the percentage of abnormally low counts were revealed in the discrete analyses of WBC count, hemoglobin, and platelet count. In addition, a marginally significant negative association was found for the percentage of abnormally high hemoglobin counts and 1987 dioxin. For the blood count measures, a marginally significant positive association was found between absolute monocytes and 1987 dioxin.

Table 15-30. Summary of 1987 Dioxin Analysis (Model 4) for Hematology Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Laboratory		
Red Blood Cell (RBC) Count (C)	NS	ns
Red Blood Cell (RBC) Count (D)		
Abnormal Low vs. Normal	ns	ns
Abnormal High vs. Normal	NS	NS
White Blood Cell (WBC) Count (C)	+0.013	NS
White Blood Cell (WBC) Count (D)		
Abnormal Low vs. Normal	–0.020	–0.032
Abnormal High vs. Normal	ns	ns
Hemoglobin (C)	NS	NS
Hemoglobin (D)		
Abnormal Low vs. Normal	–0.049	ns
Abnormal High vs. Normal	ns*	ns
Hematocrit (C)	NS	NS
Hematocrit (D)		
Abnormal Low vs. Normal	ns	ns
Abnormal High vs. Normal	NS	NS
Platelet Count (C)	+0.005	NS
Platelet Count (D)		
Abnormal Low vs. Normal	–0.028	ns
Abnormal High vs. Normal	ns	ns
Prothrombin Time (C)	ns	ns
Prothrombin Time (D)	ns	ns
RBC Morphology	NS	NS
Absolute Neutrophils (Segs) (C)	+0.017	NS
Absolute Neutrophils (Bands) (Nonzero Measurements) (C)	NS	NS
Absolute Neutrophils (Bands) (Zero vs. Nonzero) (D)	ns	ns
Absolute Lymphocytes (C)	NS	NS
Absolute Monocytes (C)	NS*	NS
Absolute Eosinophils (Nonzero Measurements) (C)	ns	ns
Absolute Eosinophils (Zero vs. Nonzero) (D)	NS	ns

Table 15-30. Summary of 1987 Dioxin Analysis (Model 4) for Hematology Variables (Ranch Hands Only) (Continued)

Variable	Unadjusted	Adjusted
Absolute Basophils (Nonzero Measurements) (C)	NS	ns
Absolute Basophils (Zero vs. Nonzero) (D)	ns	ns

Note: NS or ns: Not significant (p>0.10).
NS* or ns*: Marginally significant (0.05<p≤0.10).
C: Continuous analysis.
D: Discrete analysis.
+: Slope nonnegative for continuous analysis.
–: Relative risk <1.00 for discrete analysis.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

15.5 CONCLUSION

Five cell count measures, six measures of absolute blood counts, a coagulation measure, and RBC morphology were analyzed for the hematology assessment. In the analyses of these variables, only platelet count exhibited significant dose-response associations with the indices of dioxin exposure. Ranch Hands enlisted flyers and groundcrew exhibited slightly but significantly higher mean platelet counts than did Comparisons. Ranch Hands in the high dioxin category also exhibited a significantly higher mean platelet count than Comparisons in the continuous analysis. The results in the 1997 follow-up study parallel the findings of the 1987 and 1992 follow-up studies. In conclusion, apart from platelet count, there appears to be little evidence to support a relation between prior dioxin exposure and hematopoietic toxicity.

REFERENCES

1. McConnell, E. E., J. A. Moore, and D. W. Dalgard. 1978. Toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin in Rhesus monkeys (Macaca mulatta) following a single oral dose. *Toxicology and Applied Pharmacology* 43:175-87.
2. Kociba, R. J., P. A. Keeler, C. N. Park, and P. J. Gehring. 1976. 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). Results of a 13-week oral toxicity study in rats. *Toxicology and Applied Pharmacology* 35:553-74.
3. Weissberg, J. B., and J. G. Zinkle. 1973. Effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin upon hemostasis and hematologic function in the rat. *Environmental Health Perspectives* 5:119-23.
4. Zinkle, J. G., J. G. Vos, J. A. Moore, and B. N. Gupta. 1973. Hematologic and clinical chemistry effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin in laboratory animals. *Environmental Health Perspectives* 5:111-8.
5. Vos, J. G., J. A. Moore, and J. G. Zinkle. 1973. Toxicity of 2,3,7,8-tetrachloridibenzo-p-dioxin (TCDD) on the immune system of laboratory animals. *Environmental Health Perspectives* 5:149-62.
6. Vos, J. G., J. A. Moore, and J. G. Zinkle. 1974. Toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in C57B1/6 mice. *Toxicology and Applied Pharmacology* 29:229-41.
7. Kerkvliet, N. I., and J. A. Oughton. 1993. Acute inflammatory response to sheep red blood cell challenge in mice treated with 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD): phenotypic and functional analysis of peritoneal exudate cells. *Toxicology and Applied Pharmacology* 119:248-57.
8. Luster, M. I., L. H. Hong, G. A. Borman, G. Clark, H. T. Hayes, W. F. Greenlee, K. Dold, and A. N. Tucker. 1985. Acute myelotoxic responses in mice exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Toxicology and Applied Pharmacology* 81:156-65.
9. Tucker, A. N., S. J. Vore, and M. I. Luster. 1986. Suppression of B cell differentiation by 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Molecular Pharmacology* 29:372-7.
10. Luster, M. I., J. A. Blank, and J. H. Dean. 1987. Molecular and cellular basis of chemically induced immunotoxicity. *Annual Review of Pharmacology and Toxicology* 7:23-49.
11. Roberts, E. A., L. M. Vella, C. L. Golas, L. A. Dafoe, and A. B. Okey. 1989. Ah receptor in spleen of rodent and primate species: Detection by binding of 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Canadian Journal of Physiology and Pharmacology* 67:594-600.
12. Nebert, D. W. 1989. The Ah locus: Genetic differences in toxicity, cancer, mutation, and birth defects. *Critical Reviews in Toxicology* 20:153-74.
13. Roberts, E. A., K. C. Johnson, P. A. Harper, and A. B. Okey. 1990. Characterization of the Ah receptor mediating aryl hydrocarbon hydroxylase induction in the human liver cell line Hep G2. *Archives of Biochemistry and Biophysics* 276:442-50.
14. Choi, E., D. Toscano, J. Ryan, N. Riedel and W. J. Toscano. 1991. Dioxin induces transforming growth factor-alpha in human keratinocytes. *Journal of Biological Chemistry* 266:9591-7.
15. Waithe, W., M. Michaud, P. Harper, A. Okey, and A. Anderson. 1991. The Ah receptor, cytochrome P450IA1 mRNA induction, and aryl hydrocarbon hydroxylase in a human lymphoblastoid cell line. *Biochemical Pharmacology* 41:85-92.
16. Lorenzen, A, and A. B. Okey. 1991. Detection and characterization of Ah receptor in tissue and cells from human tonsils. *Toxicology and Applied Pharmacology* 107:203-14.

17. Harper, P., R. Prokipcak, L. Bush, C. Golas, and A. Okey. 1991. Detection and characterization of the Ah receptor for 2,3,7,8-tetrachlorodibenzo-p-dioxin in the human colon adenocarcinoma cell line LS180. *Archives of Biochemistry and Biophysics* 290:27-36.

18. Silbergeld, E. K., and T. A. Gasiewicz. 1989. Commentary: Dioxins and the Ah receptor. *American Journal of Industrial Medicine* 16:455-74.

19. Fingerhut, M. A., W. E. Halperin, D. A. Marlow, L. A. Piacitelli, P. A. Honchar, M. H. Sweeney, A. L. Greife, P. A. Dill, K. Steenland, and A. J. Suruda. 1991. Cancer mortality in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *New England Journal of Medicine* 324:212-8.

20. Ott, M. G., A. Zober, and C. Germann. 1994. Laboratory results for selected target organs in 138 individuals occupationally exposed to TCDD. *Chemosphere* 29:2423-37.

21. Moses, M., R. Lilis, K. D. Crow, J. Thornton, A. Fischbein, H. A. Anderson, and I. J. Selikoff. 1984. Health status of workers with past exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin in the manufacture of 2,4,5-trichlorophenoxyacetic acid: Comparison of findings with and without chloracne. *American Journal of Industrial Medicine* 5:161-82.

22. Stehr, P. A., G. Stein, H. Falk, E. Sampson, S. J. Smith, K. Steinberg, K. Webb, S. Ayres, W. Schramm, H. D. Donnell, and W. B. Gidney. 1986. A pilot epidemiologic study of possible health effects associated with 2,3,7,8-tetrachlorodibenzo-p-dioxin contamination in Missouri. *Archives of Environmental Health* 42:16-22.

23. Hoffman, R. E., P. A. Stehr-Green, K. B. Webb, G. Evans, A. P. Knutsen, W. F. Schramm, J. L. Staake, B. B. Gibson, and K. K. Steinberg. 1986. Health effects of long-term exposure to 2,3,7.8-tetrachlorodibenzo-p-dioxin. *Journal of the American Medical Association* 25:2031-8.

24. Evans, R. G., K. B. Webb, A. P. Knutsen, S. T. Roodman, D. W. Roberts, J. R. Bagby, W. A. Garrett, and J. S. Andrews, Jr. 1988. A medical followup of the health effects of long-term exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Archives of Environmental Health* 43:273-8.

25. Webb, K., R. G. Evans, P. Stehr, and S. M. Ayres. 1987. Pilot study on health effects of environmental 2,3,7,8-TCDD in Missouri. *American Journal of Industrial Medicine* 11:685-91.

26. Webb, K. B., R. G. Evans, A. P. Knutsen, and S. T. Roodman. 1989. Medical evaluation of subjects with known body levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Journal of Toxicology and Environmental Health* 28:183-93.

27. Suskind, R. R., and V. S. Hertzberg. 1984. Human health effects of 2,4,5-T and its toxic contaminants. *Journal of the American Medical Association* 251:2372-80.

28. Pocchiari, F., V. Silano, and A. Zampieri. 1979. Human health effects from accidental release of tetrachlorodibenzo-p-dioxin (TCDD) at Seveso, Italy. *Annals of the New York Academy of Sciences* 320:311-20.

29. May, G. 1973. Chloracne from the accidental production of tetrachlorodibenzodioxin. *British Journal of Industrial Medicine* 30:276-83.

30. Bertazzi, P., C. Zocchetti, A. Pesatori, S. Guercilena, D. Consonni, A. Tironi, and M. Landi. 1992. Mortality of a young population after accidental exposure to 2,3,7,8-tetrachlorodibenzodioxin. *International Journal of Epidemiology* 21:118-23.

31. Bertazzi, P. A., C. Pesatori, D. Consonni, A. Tironi, M. T. Landi, and C. Zocchetti. 1993. Cancer incidence in a population accidentally exposed to tetrachlorodibenzo-para-dioxin. *Epidemiology* 4:398-406.

32. Collins, J.J., M.E. Strauss, G.J. Levinskas, and P. R. Conner. 1993. The mortality experience of workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin in a trichloropheno-process accident. *Epidemiology* 4:7-13.

33. Assennato, G., P. Cannatelli, E. Emmett, I. Ghezzi, and F. Merlo. 1989. Medical monitoring of dioxin clean-up workers. *American Industrial Hygiene Association Journal* 50:586-92.

34. Centers for Disease Control. 1989. Health status of Vietnam veterans. *Vietnam Experience Study*. Atlanta: U.S. Department of Health and Human Services. Vols. I-V, Supplements A-C.

35. Lathrop, G. D., W. H. Wolfe, R. A. Albanese, and P. M. Moynahan. 1984. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Baseline Morbidity Study Results. NTIS: AD A-138-340. United States Air Force School of Aerospace Medicine, Brooks Air Force Base, Texas.

36. Lathrop, G. D., S. G. Machado, T. G. Karrison, W. D. Grubbs, W. F. Thomas, W. H. Wolfe, J. E. Michalek, J. C. Miner, and M. R. Peterson. 1987. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: First followup examination results. NTIS: AD A 188262. United States Air Force School of Aerospace Medicine, Brooks Air Force Base, Texas.

37. Thomas, W. F., W. D. Grubbs, T. G. Karrison, M. B. Lustik, R. H. Roegner, D. E. Williams, W. H. Wolfe, J. E. Michalek, J. C. Miner, and R.W. Ogershok. 1990. An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: I. 1987 followup examination results, May 1987 to January 1990. NTIS: AD A 222 573. United States Air Force School of Aerospace Medicine, Human Systems Division (AFSC), Brooks Air Force Base, Texas.

38. Roegner, R. H., W. D. Grubbs, M. B. Lustik, A. S. Brockman, S. C. Henderson, D. E. Williams, W. H. Wolfe, J. E. Michalek, and J. C. Miner. 1991. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides. Serum dioxin analysis of 1987 examination results. NTIS: AD A 237 516-24. United States Air Force School of Aerospace Medicine, Brooks Air Force Base, Texas.

39. W. D. Grubbs, W. H. Wolfe, J. E. Michalek, D. E. Williams, M. B. Lustik, A. S. Brockman, S. C. Henderson, F. R. Burnett, R. G. Land, D. J. Osborne, V. K. Rocconi, M. E. Schreiber, J. C. Miner, G. L. Henriksen, and J. A. Swaby. 1995. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final Report. 1992 Followup Examination Results. NTIS: AD A 304 306, 304 308-316. United States Air Force School of Aerospace Medicine, Brooks Air Force Base, Texas.

40. Michalek, J. E., J. L. Pirkle, S. P. Caudill, R. C. Tripathi, D. G. Patterson Jr., and L. L. Needham. 1996. Pharmacokinetics of TCDD in Veterans of Operation Ranch Hand: 10-year Followup. *Journal of Toxicology and Environmental Health* 47:209-20.

41. Mausner, J. S., and A. K. Bahn. 1974. *Epidemiology – An Introductory Text*. Philadelphia: W. B. Saunders Company.

Table of Contents

List of Tables

16 ENDOCRINE ASSESSMENT

16.1 INTRODUCTION

16.1.1 Background

The essential role of membrane and intracellular receptors in human endocrine function has been firmly established and extensively studied (1). In animal models, much of the basic research into the mechanism of dioxin endocrine toxicity has focused on the dioxin-binding aryl hydrocarbon (Ah) receptor, which has similarities to the endocrine receptors that mediate function of the thyroid, adrenal, and gonadal hormones (2-5).

Animal research has documented that the thyroid is a target organ for dioxin toxicity, although the mechanism has not been defined clearly (6-11). In other studies, dioxin-induced changes in thyroid indices (serum thyroxine [T_4], triiodothyronine [T_3], and thyroid stimulating hormone [TSH]) were directionally different with species and strain specificity (12, 13). The mechanism by which dioxin interacts with or regulates thyroid function in experimental animals remains under investigation. In competing for thyroid hormone binding sites in target organs (14) or by accelerating the metabolism of thyroid hormones by hepatic enzyme induction (15), dioxin administration can induce a mildly hypothyroid state associated with elevated levels of TSH.

How these experimental studies relate to the effect of dioxin on human thyroid function has not been established. The most recently published morbidity reports on the workers exposed to dioxin during a chemical factory explosion in Germany in 1953 included thyroid disorders in the analyses. Across all exposure categories, an increased incidence of thyroid disease was found in workers relative to referents (16). Thyroid disease occurred in 11 of 158 in the exposed cohort but in only two of 161 referents. The heterogeneous mix of thyroid disorders—four cases of thyrotoxicosis, four cases of goiter, two cases of hypothyroidism, and one other unspecified disorder—weighs against a possible relation with dioxin exposure. In the analyses of laboratory measurements from the same exposed population, the authors found positive associations between each of the exposure indices and selected tests of thyroid function, T_4, and thyroxine binding globulin (17). Unfortunately, the most widely used measure of thyroid function—serum TSH—was not included in the analyses.

The finding in laboratory animals of physicochemical similarities between the dioxin-binding Ah and glucocorticoid receptors (5, 18) has prompted further investigation into the interaction of dioxin with other steroid hormones. A review by Couture, et al. (19) provided a comprehensive summary of the research into the developmental toxicity and teratogenicity of dioxin in experimental animals.

Experimental studies have documented numerous adverse male reproductive effects in laboratory animals exposed to dioxin, including reduced testicular weight, impaired spermatogenesis, decreased testicular testosterone secretion, and atrophy of the androgen-sensitive seminal vesicles and epididymis (20-24). Although dioxin administration is associated with diminished testosterone secretion in rats (23, 25, 26), the mechanism is unknown and may involve the hypothalamic-pituitary axis. In rats, dioxin inhibits the secretion of luteinizing hormone (LH) by the pituitary gland, an effect associated with androgen deficiency (27, 28). In other experiments, dioxin inhibited the response of the pituitary to gonadotropin-releasing hormone secreted by the hypothalamus (29).

Additional experiments have explored the effects of dioxin on the pituitary and hypothalamus (30, 31). The use of microsurgical techniques in female rats revealed that dioxin toxicity is aggravated by hypophysectomy, with a sparing effect noted upon administering either corticosterone or thyroid hormone (30). Another study defined a biochemical basis for the effect of dioxin on prolactin levels controlled by the adenohypophysis in female rats (32). Studies on the effects of dioxin on the pituitary-adrenal axis have documented significant suppression of corticosterone production by the adrenal gland (33) and defined a biochemical basis for the apparent reduction in bioactivity of adrenocorticotropic hormone secreted by the pituitary (34).

The National Institute for Occupational Safety and Health (NIOSH) has conducted several long-term epidemiological studies of factory workers who experienced significant occupational exposure to dioxin in chemical production plants (35, 36). In their most recently published report (37), serum levels of three endocrine indices—testosterone, LH, and follicle stimulating hormone (FSH)—were examined in relation to current and calculated initial serum dioxin levels in 248 participants. Current serum dioxin levels were positively and significantly related to both LH and FSH and inversely related to testosterone. In contrast to the NIOSH results, a recent report of the Air Force Health Study (AFHS) population found no relation between the body burden of dioxin and reproductive or endocrine indices, including serum testosterone, FSH, LH, sperm counts and morphology, and anatomic abnormalities of the testes (38).

The possibility that dioxin might affect glucose metabolism in humans was first raised in 1981 with the publication of an occupational study that reported an unusually high prevalence of abnormal glucose tolerance tests (40%) and a 20-percent incidence of diabetes in chemical production workers exposed to dioxin (39). The results of analyses pertinent to glucose metabolism based on serum dioxin data collected during the 1987 and 1992 AFHS examinations recently have been published (40). In the 1987 examination, Ranch Hand participants with the highest serum dioxin levels were nearly three times as likely to have elevations in fasting blood sugar than were Comparisons (41). In the 1992 examination, Ranch Hand participants with high levels of serum dioxin had significantly higher fasting and 2-hour postprandial glucose results than those with lower levels of serum dioxin (42), an effect that was shown to be independent of the serum triglyceride level (43). In nondiabetic Ranch Hands, serum insulin, like the 2-hour postprandial glucose, was positively and significantly associated with current serum dioxin levels. In contrast, in diabetic participants, a consistent inverse dose-response effect was found in all models relating serum insulin to current serum dioxin. Although cause and effect have not been established, these results provide further evidence for an association between glucose intolerance and dioxin levels and raise the possibility that, in a subset of those predisposed to diabetes, dioxin may impair insulin production.

Whether dioxin exposure is in fact a risk factor for the development of diabetes remains controversial. Recent reports from NIOSH noted statistically significantly associations between the prevalence of diabetes and elevated fasting blood sugar with increasing serum dioxin levels (44), although the authors could not exclude confounding by the traditional diabetic risk factors of age, obesity, and family history of diabetes. Other epidemiological studies, some of which have included serum dioxin levels in the analyses, have failed to find an association between glucose intolerance and exposure to dioxin (16, 17, 45).

In the most recent publication by the Institute of Medicine, a special section is devoted to the subject of dioxin exposure as a risk factor for the development of diabetes (46). Based on its comprehensive review of the literature, the committee concluded that "at this time, there is inadequate/insufficient evidence to determine whether an association exists between herbicide or dioxin exposure and increased risk of diabetes."

16.1.2 Summary of Previous Analyses of the Air Force Health Study

16.1.2.1 1982 Baseline Study Summary Results

A laboratory evaluation of the endocrine system was used for analysis in the baseline examination in 1982. Five measures of endocrine status were assessed: T_3 percent uptake, T_4, free thyroxine index (FTI), testosterone, and 2-hour postprandial glucose.

Results showed significant group differences for T_3 percent uptake (abnormally low), predominantly in Ranch Hands 40 years old or younger. The highest percentage of abnormalities was in participants with high body fat. No group difference was noted for elevated 2-hour postprandial glucose values and, as expected, the prevalence of abnormal values was associated with increased age and higher body fat. Lower testosterone values also were associated with increased age and higher body fat. Higher mean testosterone values were significantly more prevalent in the Ranch Hand group. Significant mean shifts were not noted for the T_3 percent uptake, T_4, and the FTI.

These data, coupled with the animal literature on the profound influence of the endocrine system on lethality and body fat metabolism following dioxin exposure, clearly underscored the importance of a more comprehensive evaluation of the endocrine system.

16.1.2.2 1985 Follow-up Study Summary Results

Questionnaire and review-of-systems data for past thyroid disease were similar in both the Ranch Hand and Comparison groups. These historical data were confirmed by a medical records review. Physical examination findings were necessarily limited to data from palpation of the thyroid gland and testicles; the unadjusted results showed no significant group differences.

Evaluation of the endocrine system was conducted primarily by laboratory testing. The thyroid test battery consisted of T_3 percent uptake and TSH, as determined by radioimmunoassay techniques. Testosterone, initial cortisol, differential cortisol (the difference between the initial and 2-hour cortisol levels), and 2-hour postprandial glucose levels also were analyzed. The T_3 percent uptake data showed no group differences for either mean values or frequency of abnormally low or high values. TSH results revealed a significantly higher mean level in the Ranch Hand group, but this difference was not detected by discrete analysis of the proportions of abnormally high TSH results.

The mean level of testosterone remained significantly elevated for Ranch Hands, as contrasted with Comparisons, in the 10 to 25 percent body fat category, but this difference was not reflected in the discrete analyses. For the few participants with less than 10 percent body fat (six Ranch Hands, four Comparisons), mean testosterone levels were lower for Ranch Hands than for Comparisons.

Two timed cortisol specimens showed no significant group differences in mean values or the percentage of participants with abnormalities. The difference between the timed cortisol results, termed the "differential cortisol," showed no significant group differences for non-Blacks or Blacks born before 1942, but Black Ranch Hands born in or after 1942 had a lower mean differential cortisol level than did their Comparisons.

Group means of 2-hour postprandial glucose levels were not statistically different, but discrete analyses revealed that there was a significantly higher frequency of glucose-impaired (at least 140 mg/dl, but less than 200 mg/dl) Comparisons than Ranch Hands. A variable comprising known diabetics and individuals classified as diabetic by the glucose tolerance test showed no difference between the Ranch Hand and

Comparison groups. The covariates age, race, and body fat were significantly associated with diabetes in this analysis.

16.1.2.3 1987 Follow-up Study Summary Results

The endocrine assessment did not disclose any statistically significant differences between the Ranch Hand and Comparison groups. The percentage of participants who indicated problems with current thyroid disease was similar between groups, as were the percentages with thyroid and testicular abnormalities determined by palpation at the physical examination. The Ranch Hand TSH mean was marginally significantly higher than the Comparison TSH mean. Ranch Hand and Comparison mean levels were similar for T_3 percent uptake, FSH, testosterone, and 2-hour postprandial glucose. The percentage of Ranch Hands with abnormal values for these five laboratory variables was higher than the percentage of Comparisons with abnormal values; however, the difference in the percentage of abnormal values between Ranch Hands and Comparisons was not statistically significant for these five laboratory variables. In addition, analyses were performed on a composite diabetes indicator. A participant was considered diabetic for this indicator if he had a verified history of diabetes or had a 2-hour postprandial glucose level of at least 200 mg/dl. The difference in the percentage of Ranch Hands and Comparisons considered diabetic, as determined through this composite diabetes indicator, was not significant.

16.1.2.4 Serum Dioxin Analysis of 1987 Follow-up Study Summary Results

The endocrine assessment found a strong positive association between initial dioxin and diabetes prevalence and testes abnormalities; however, the analyses of current dioxin levels in Ranch Hands and Comparisons indicated that the increased risk was apparent only for Ranch Hands in the high current dioxin category (>33.3 parts per trillion [ppt]). These Ranch Hands also had significantly higher mean levels of TSH, fasting glucose, and 2-hour postprandial glucose than background Comparisons, as well as lower mean levels of T_3 percent uptake and testosterone. The discrete analyses of these variables found a significant increase in abnormally elevated fasting glucose levels and diabetic 2-hour postprandial glucose levels as both initial dioxin and current dioxin increased.

16.1.2.5 1992 Follow-up Study Summary Results

The assessment of the endocrine system included an extensive evaluation of thyroid, pancreatic, and gonadal functions and their relation to dioxin exposure. Analyses of thyroid functions did not identify significant differences between Ranch Hands and Comparisons. Similarly, the prevalence of diabetes in the two populations was not significantly different, although significant positive associations were found between time to the onset of diabetes and both lipid-adjusted and whole weight dioxin levels, as measured in 1987.

Significant glucose metabolism results were confined to the current serum dioxin analyses. These results suggested a possible mechanism for dioxin effect on glucose metabolism and the development of diabetes. Diabetic Ranch Hands with high levels of current serum dioxin had significantly higher fasting glucose levels than those with lower levels of dioxin. Nondiabetic Ranch Hands, on the other hand, exhibited an inverse association between fasting glucose and current serum dioxin and a positive association between 2-hour postprandial glucose and current serum dioxin. Serum dioxin levels were significantly related to elevated insulin levels in nondiabetic, but not in diabetic Ranch Hands. This was suggestive of a dioxin effect on glucose metabolism with a heightened release of insulin in Ranch Hands with a fully responsive pancreas. When this pancreatic response is no longer effective, elevated glucose levels lead to the clinical diagnosis of diabetes and loss of the dose-response between dioxin and insulin.

Analyses of gonadal functions detected a significant inverse dose-response relation between current serum dioxin and total serum testosterone in Ranch Hands. These results supported those described in the Serum Dioxin Analysis of the 1987 Follow-up Examination, but the clinical meaning was uncertain.

In conclusion, although the existence of endocrine disorders was comparable in Ranch Hands and Comparisons, the assessment of glucose metabolism showed the possibility of adverse effects from dioxin in relation to glucose intolerance and insulin production.

16.1.3 Parameters for the 1997 Endocrine Assessment

16.1.3.1 Dependent Variables

Questionnaire, physical examination, and laboratory data collected at the AFHS 1997 follow-up examination were used in the endocrine assessment. The self-reported information collected from the 1997 questionnaire was subsequently verified and analyses were based on the verified data.

16.1.3.2 Medical Records Data

The 1997 questionnaire posed a general screening question on thyroid function and disease. Each participant was asked the following question during the in-person health interview: "Since the date of the last interview, has a doctor told you for the first time that you had thyroid problems?" All affirmative responses were verified by a medical records review and added to previously reported and verified information on the thyroid function from the 1982 baseline examination and the 1985, 1987, and 1992 follow-up examinations for each participant. Thyroid disease was classified according to the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) diagnostic codes. The ICD-9-CM codes for thyroid disease encompassed 240.0-246.9. Based on the verified data, history of thyroid disease was classified as "yes" or "no." Participants with a pre-Southeast Asia (SEA) history of thyroid disease were excluded from the analysis of thyroid disease history.

Similar information was asked of each participant regarding diabetes. This information also was verified and combined with previous information. ICD-9-CM codes 250.00-250.93 were used to classify diabetes. Participants with a verified history of diabetes were combined with those participants with a 2-hour postprandial glucose level of 200 mg/dl or greater at the 1997 physical examination and classified as "yes" for a composite diabetes indicator variable. Those participants without a verified history of diabetes and with a 2-hour postprandial glucose level of less than 200 mg/dl at the 1997 physical examination were classified as "no." This composite diabetes indicator, derived from a medical records review and laboratory results, was analyzed as part of the endocrine assessment. Participants classified as "yes" were designated as diabetics and participants classified as "no" were designated as nondiabetics.

After the data were analyzed, medical records of all participants designated as diabetic, based on medical records, were reviewed to determine diabetic type (1 or 2). One participant (a Ranch Hand veteran) was diagnosed as having type 1 (insulin-dependent) diabetes and the remainder were diagnosed as having type 2 (adult onset) diabetes. A reanalysis with the single Ranch Hand with type 1 diabetes excluded yielded the same results as those already presented.

As part of the 1997 questionnaire, questions were asked of diabetics regarding the use of insulin, oral diabetes medication, and diet. This self-reported information was verified and a diabetic severity index was constructed and analyzed for all participants. This index was categorized as "requiring insulin," "oral hypoglycemic," "diet only," or "no treatment" for diabetics and "no diabetes" for nondiabetics.

The date on which a participant was first diagnosed with diabetes was used to measure a time to diabetes onset by determining the number of years between the date of diagnosis and the end date of the last tour of duty in SEA. Time to diabetes onset for those participants who have not been diagnosed with diabetes was the number of years between the 1997 examination date and the end date of the last tour of duty in SEA. This method of determining time to diabetes onset also was used for participants with a 2-hour postprandial glucose level of 200 mg/dl or greater at the 1997 physical examination but not yet diagnosed with diabetes.

Participants with a pre-SEA history of diabetes were excluded from the analyses of the composite diabetes indicator, diabetic severity, and time to diabetes onset.

16.1.3.2.1 Physical Examination Data

The physical examination of endocrine function included manual palpation of the thyroid gland and testes. Thyroid abnormalities consisted of enlarged gland, tenderness, presence of nodules, or thyroidectomies. Testicular abnormalities consisted of atrophied or absent testes. Participants with a pre-SEA history of thyroid disease and participants who are currently taking thyroid medication were excluded from the analysis of the thyroid gland. For the analysis of testicular abnormalities, participants with pre-SEA orchiectomies or participants with a missing testicle because of an undescended testicle or a congenital absence were excluded.

16.1.3.2.2 Laboratory Examination Data

For the 1997 follow-up examination, 14 laboratory variables were analyzed statistically in the endocrine assessment for all participants. TSH (μIU/ml), thyroxine (μg/dl), LH (mIU/ml), FSH (mIU/ml), and total testosterone (ng/dl) were conducted using Ciba Corning ACS 180® equipment. Abbott IMX® equipment was used to measure α-1-C hemoglobin (percent) and estradiol (pg/ml). Measurements for fasting glucose (mg/dl) were taken using Dade RxL® equipment. Fasting urinary glucose analyses were conducted by dipstick methods using Bayer Atlas® equipment. Anti-thyroid antibodies were analyzed using passive hemagglutination assay. Free testosterone (pg/ml) was conducted by radioimmunoassay.

In addition, the analyses of 2-hour postprandial glucose (mg/dl), serum insulin (μIU/ml), and the presence of 2-hour postprandial urinary glucose were restricted to nondiabetics only. Measurements for 2-hour postprandial glucose (mg/dl) were taken using Dade RxL® equipment. Analyses for 2-hour postprandial urinary glucose were conducted by dipstick methods using Bayer Atlas® equipment. Abbott IMX® equipment was used to measure serum insulin. The 100-gram glucose load for the postprandial assays was standardized by the use of Glucola® and was not given to diabetics unless requested by the participant.

All laboratory variables were analyzed in both discrete and continuous forms except for anti-thyroid antibodies, fasting urinary glucose, and 2-hour postprandial urinary glucose. These variables were analyzed as discrete variables only and categorized as "present" or "absent."

TSH and serum insulin were categorized as "abnormally low," "normal," and "abnormally high." The results for 2-hour postprandial glucose were coded as "normal" and "impaired." All other laboratory results were dichotomized as "normal" or "abnormal" (abnormally high for all variables, except for thyroxine, total testosterone, and free testosterone, which were classified according to abnormally low values).

Participants with thyroidectomies, a pre-SEA history of thyroid disease, or who are taking thyroid medication were excluded from the analyses of TSH, thyroxine, and anti-thyroid antibodies. For total and free testosterone, participants with orchiectomies (pre-SEA or post-SEA), participants with a missing testicle because of an undescended testicle or a congenital absence, and participants currently taking testosterone medication were excluded. Participants with pre-SEA diabetes were excluded from the analysis of fasting glucose, fasting urinary glucose, and α-1-C hemoglobin. Participants who were diabetic (pre-SEA and post-SEA) or participants with a 2-hour postprandial glucose level greater than or equal to 200 mg/dl were excluded from the analyses of 2-hour postprandial glucose, 2-hour postprandial urinary glucose, and serum insulin.

As described above, a 100-gram glucose load for the postprandial assays was standardized by the use of Glucola®. Some participants were not given Glucola® by request. A subset of these participants was not classified as diabetic through a medical records review; their 2-hour postprandial glucose was less than 200 mg/dl without consuming the Glucola®. Consequently, these participants could not be classified as diabetic or nondiabetic for the composite diabetes indicator and were considered to have an unknown diabetic status. These participants were excluded from analyses of 2-hour postprandial glucose, 2-hour postprandial urinary glucose, and serum insulin.

16.1.3.3 Covariates

The endocrine assessment included the effects of age, race, and military occupation in the adjusted analyses of all variables. To adjust for the effects of stress on endocrinologic measures, personality type was used as an additional covariate for past thyroid disease, thyroid gland abnormalities, TSH, thyroxine, and anti-thyroid antibodies. Age, race, occupation, personality type, and body fat were included in the adjusted analyses of the testes-related variables (testicular examination, total testosterone, and free testosterone). A covariate characterizing family history of diabetes was included for the diabetes-related variables, along with age, race, military occupation, personality type, and body fat. These dependent variables included the composite diabetes indicator, diabetic severity, time to diabetes onset, fasting and 2-hour postprandial glucose, fasting and 2-hour postprandial urinary glucose, serum insulin, and α-1-C hemoglobin.

Age, race, and military occupation were determined from military records. Personality type was determined from the Jenkins Activity Survey administered during the 1997 follow-up examination and was derived from a discriminant-function equation based on questions that best discriminate men judged to be type A from those judged to be type B (47). Positive scores reflected the type A direction; negative scores reflected the type B direction. Personality type was dichotomized as type A or type B.

Body fat was calculated from a metric body mass index (48); the formula is

$$\textit{Body Fat (in percent)} = \frac{\textit{Weight (kg)}}{[\textit{Height (m)}]^2} \bullet 1.264 - 13.305.$$

Each participant was asked in the 1997 questionnaire whether anyone in his immediate family ever had diabetes or sugar diabetes. A family history of diabetes covariate was constructed from this question and used in adjusted analyses of all diabetic-related dependent variables.

16.1.4 Statistical Methods

Table 16-1 summarizes the statistical analysis that was performed for the endocrine assessment. The first part of this table describes the dependent variables and identifies the covariates and the statistical

methods. The second part of this table further describes the covariates. A covariate was used in its continuous form whenever possible for all adjusted analyses. If the covariate was inherently discrete (e.g., military occupation), or if a categorized form was needed to develop measures of association, the covariate was categorized as shown in Table 16-1. Table 16-2 provides a summary of the number of participants with missing dependent variable and covariate data. In addition, the number of participants excluded because of medical conditions is given.

Table 16-1. Statistical Analysis for the Endocrine Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
Past Thyroid Disease	MR-V	D	Yes No	(1)	(a)	U:LR A:LR
Composite Diabetes Indicator	MR-V/ LAB	D	• Diabetic: Verified History or ≥200 mg/dl 2-hr. post-prandial glucose • Nondiabetic: Otherwise	(2)	(b)	U:LR A:LR L:LR
Diabetic Severity	MR-V	D	Requiring Insulin Oral Hypoglycemics Diet Only No Treatment No Diabetes	(2)	(b)	U:PR A:PR
Time to Diabetes Onset (years)	MR-V/ LAB/ MIL	C	--	(2)	(b)	U:ST A:ST
Thyroid Gland	PE	D	Abnormal Normal	(1)	(c)	U:LR A:LR
Testicular Examination	PE	D	Abnormal Normal	(3)	(d)	U:LR A:LR
TSH (μIU/ml)	LAB	D/C	Abnormal Low: <0.35 Normal: 0.35-5.5 Abnormal High: >5.5	(1)	(e)	U:PR,GLM A:PR,GLM L:PR,GLM
Thyroxine (T_4) (μg/dl)	LAB	D/C	Low: <4.8 Normal: ≥4.8	(1)	(e)	U:LR,GLM A:LR,GLM
Anti-Thyroid Antibodies	LAB	D	Present Absent	(1)	(e)	U:LR A:LR
Fasting Glucose (mg/dl)	LAB	D/C	High: >110 Normal: ≤110	(2)	(b)	U:LR,GLM A:LR,GLM L:LR,GLM
2-Hour Postprandial Glucose (mg/dl)	LAB	D/C	Impaired: 140-<200 Normal: <140	(2)	(f)	U:LR,GLM A:LR,GLM L:LR,GLM

Table 16-1. Statistical Analysis for the Endocrine Assessment (Continued)

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
Fasting Urinary Glucose	LAB	D	Present Absent	(2)	(b)	U:LR A:LR
2-Hour Postprandial Urinary Glucose	LAB	D	Present Absent	(2)	(f)	U:LR A:LR
Serum Insulin (μIU/ml)	LAB	D/C	Abnormal Low: <18 Normal: 18-56 Abnormal High: >56	(2)	(f)	U:PR,GLM A:PR,GLM
α-1-C Hemoglobin (percent)	LAB	D/C	High: >7.7 Normal: ≤7.7	(2)	(b)	U:LR,GLM A:LR,GLM
Total Testosterone (ng/dl)	LAB	D/C	Low: <241 (Ages 45-49) <230 (Age ≥50) Normal: ≥241 (Ages 45-49) ≥230 (Age ≥50)	(3)	(g)	U:LR,GLM A:LR,GLM L:LR,GLM
Free Testosterone (pg/ml)	LAB	D/C	Low: <6 Normal: ≥6	(3)	(g)	U:LR,GLM A:LR,GLM
Estradiol (pg/ml)	LAB	D/C	High: >50 Normal: ≤50	(4)	None	U:LR,GLM A:LR,GLM
LH (mIU/ml)	LAB	D/C	High: >9.3 Normal: ≤9.3	(4)	None	U:LR,GLM A:LR,GLM
FSH (mIU/ml)	LAB	D/C	High: >15 Normal: ≤15	(4)	None	U:LR,GLM A:LR,GLM

[a]Covariates:
(1): age, race, military occupation, personality type.
(2): age, race, military occupation, personality type, body fat, family history of diabetes.
(3): age, race, military occupation, personality type, body fat.
(4): age, race, military occupation.

[b]Exclusions:
(a): participants with a pre-SEA history of thyroid disease.
(b): participants with a pre-SEA history of diabetes.
(c): participants with a pre-SEA history of thyroid disease, participants currently taking thyroid medication.
(d): participants with a pre-SEA orchiectomy, participants with a testicle absent (undescended or congenital absence).
(e): participants with a pre-SEA history of thyroid disease, participants with a thyroidectomy, participants currently taking thyroid medication.
(f): all diabetics (pre- and post-SEA), participants whose diabetic status was unknown at the 1997 physical examination.
(g): participants with an orchiectomy (pre-SEA or post-SEA), participants with a testicle absent (undescended or congenital absence), participants currently taking testosterone medication.

Table 16-1. Statistical Analysis for the Endocrine Assessment (Continued)

Covariates

Variable (Units)	Data Source	Data Form	Cutpoints
Age (years)	MIL	D/C	Born ≥1942 Born <1942
Race	MIL	D	Black Non-Black
Occupation	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Personality Type	PE	D	A direction B direction
Body Fat (percent)	PE	D/C	Obese: >25% Lean or Normal: ≤25%
Family History of Diabetes	Q-SR	D	Yes No

Abbreviations

Data Source:
LAB: 1997 laboratory results
MIL: Air Force military records
MR-V: Medical records (verified)
PE: 1997 physical examination
Q-SR: 1997 health questionnaire (self-reported)

Data Form:
C: Continuous analysis only
D: Discrete analysis only
D/C: Discrete and continuous analyses for dependent variables; appropriate form for analysis (either discrete or continuous) for covariates

Statistical Analysis:
U: Unadjusted analysis
A: Adjusted analysis
L: Longitudinal analysis

Statistical Methods:
GLM: General linear models analysis
LR: Logistic regression analysis
PR: Polytomous logistic regression analysis
ST: Survival time analysis

Cutpoints for total testosterone were age-dependent. Consequently, normal and abnormal levels for total testosterone were constructed according to a participant's laboratory value and age at the physical examination. The age-specific cutpoints are listed in Table 16-1; the reference ages for these cutpoints are given in parentheses following the cutpoints.

The analysis of time to diabetes onset was based on a regression analysis of time to onset in which time to onset was modeled as a linear combination of exposure variables and covariates. Further details on the statistical procedures used for the analysis of time to onset are discussed in Chapter 7, Statistical Methods.

Table 16-2. Number of Participants Excluded or with Missing Data for the Endocrine Assessment

Variable	Variable Use	Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
		Ranch Hand	Comparison	Initial	1987	Ranch Hand	Comparison
Composite Diabetes Indicator	DEP	9	18	5	7	7	17
Diabetic Severity	DEP	9	18	5	7	7	17
Time to Diabetes Onset	DEP	9	18	5	7	7	17
Testicular Examination	DEP	1	0	0	1	1	0
2-hour Postprandial Glucose	DEP	1	2	1	1	1	2
2-hour Postprandial Urinary Glucose	DEP	3	5	2	3	3	5
Serum Insulin	DEP	1	2	1	1	1	2
Personality Type	COV	3	0	1	3	3	0
Family History of Diabetes	COV	7	12	4	7	7	12
Pre-SEA Thyroid Disease	EXC	7	5	4	7	7	5
Pre-SEA Diabetes	EXC	2	1	2	2	2	1
Taking Thyroid Medication	EXC	24	44	13	24	24	44
Diabetic or Diabetic Status Unknown	EXC	156	228	113	152	152	217
Pre-SEA Orchiectomy	EXC	2	2	1	2	2	2
Thyroidectomy	EXC	12	15	5	12	12	15
Pre- or Post-SEA Orchiectomy	EXC	8	5	4	8	8	5
Testicle Undescended or Congenitally Absent	EXC	6	13	3	6	6	13
Taking Testosterone Medication	EXC	6	7	3	5	5	7

Note: DEP = Dependent variable.
COV = Covariate.
EXC = Exclusion.
870 Ranch Hands and 1,251 Comparisons.
482 Ranch Hands for initial dioxin; 863 Ranch Hands for 1987 dioxin.
863 Ranch Hands and 1,213 Comparisons for categorized dioxin.

16.2 RESULTS

16.2.1 Dependent Variable-Covariate Associations

The associations between the dependent variables examined in the endocrine assessment and the covariates used in the adjusted analysis were investigated. The results are presented in Appendix F, Table F-8. These associations are pairwise between the dependent variable and the covariate and are not adjusted for any other covariates. Participants were excluded from each of the analyses as given in Table 16-1. Statistically significant associations are discussed below.

The covariate tests of association for past thyroid disease revealed a significant positive association with age (p=0.020).

A participant with a verified history of diabetes or a 2-hour postprandial glucose level of greater than or equal to 200 mg/dl was considered diabetic in the composite diabetes indicator variable. The covariate

tests of association revealed age (p=0.001), race (p=0.011), personality type (p=0.001), body fat (p=0.001), and family history of diabetes (p=0.001) to be associated significantly with the composite diabetes indicator. The percentage of diabetic participants increased with age. A higher percentage of Black participants than non-Black participants were diabetic (25.6% versus 16.4%). The percentage of diabetic participants was higher for participants with type B personalities than participants with type A personalities (19.5% versus 13.0%). A higher percentage of obese participants were diabetic than lean and normal participants (28.6% versus 12.1%). A greater percentage of participants with a family history of diabetes were diabetic, relative to participants with no family history of diabetes (24.9% versus 14.1%).

Tests of covariate association revealed age (p=0.001), race (p=0.023), personality type (p=0.001), body fat (p=0.001), and family history of diabetes (p=0.001) to be significantly associated with diabetic severity. The percentage of nondiabetic participants was greater for younger participants, non-Blacks, those with a type A personality, lean participants, and participants with no family history of diabetes. The percentages of older participants who used no treatment, diet, oral hypoglycemics, and insulin to treat diabetes were 6.2, 2.5, 7.5, and 2.6, respectively. Percentages for younger participants were smaller than for older participants for all forms of treatment. The analysis of race showed that for Black participants, 7.2 percent used no treatment, 2.4 percent used diet only as a form of treatment, 11.2 percent used oral hypoglycemics, and 3.2 percent used insulin. For all forms of treatment, the percentages of non-Black participants were smaller than for Black participants. Covariate analyses revealed that 4.3 percent, 1.1 percent, 3.5 percent, and 2.1 percent of participants with type A personalities used no treatment, diet, oral hypoglycemics, and insulin, respectively, to treat their disorder. For participants with type B personalities, 6.3 percent, 2.1 percent, 6.8 percent, and 1.9 percent, respectively, used these methods in the treatment of diabetes. Of the obese participants, 9.9 percent used no treatment, 2.1 percent used diet as a form of treatment, 10.2 percent used oral hypoglycemics, and 2.1 percent used insulin. The percentages of lean or normal participants using these methods were less for each form of treatment. Of the participants with a family history of diabetes, 7.5 percent used no treatment, 2.2 percent used diet to treat their disorder, 9.1 percent used hypoglycemics, and 3.5 percent used insulin. The percentages of participants with no family history of diabetes using these methods were less for each form of treatment.

Time to diabetes onset was associated significantly with age (p<0.001), race (p=0.007), personality type (p<0.001), body fat (p<0.001), and family history of diabetes (p<0.001). Time to diabetes onset decreased significantly with increases in age and body fat. Black participants had a shorter time to diabetes onset than did non-Black participants. Participants with type A personalities had a significantly longer time to diabetes onset than did participants with type B personalities. Participants with a family history of diabetes had a significantly shorter time to diabetes onset than did participants with no family history of diabetes.

Abnormalities of the thyroid gland were significantly associated with occupation (p=0.019). Officers had the highest percentage of participants with abnormal thyroid glands (1.9%), followed by enlisted flyers (0.6%), then enlisted groundcrew (0.5%).

Tests of covariate association showed the percentage of abnormal testicular examinations to be significantly associated with age (p=0.001) and occupation (p=0.021). Older participants had a higher percentage of abnormal testicular examinations than did younger participants (6.2% versus 1.4%). Officers had the highest percentage of abnormal testicular examinations (5.2%), followed by enlisted flyers (5.1%), then enlisted groundcrew (2.8%).

TSH in its continuous form increased significantly with age (p<0.001). Race and occupation also were significant (p<0.001 and p=0.007). Non-Black participants had a higher mean TSH level than did Black

participants (1.87 μIU/ml versus 1.38 μIU/ml). Officers had the highest mean TSH level (1.94 μIU/ml), followed by enlisted groundcrew (1.78 μIU/ml), then enlisted flyers (1.77 μIU/ml). No significant covariate associations were seen with TSH in its discrete form.

Thyroxine in its continuous form was significantly associated with occupation ($p<0.001$). Enlisted flyers had the highest mean thyroxine level (7.26 μg/dl), followed by enlisted groundcrew (7.20 μg/dl), then officers (6.81 μg/dl). Tests of covariate associations with thyroxine in its discrete form revealed no significant associations.

Fasting glucose in its continuous form increased with age ($p<0.001$) and body fat ($p<0.001$). Occupation ($p=0.039$), personality type ($p=0.001$), and family history of diabetes ($p<0.001$) also were associated significantly with fasting glucose. Enlisted flyers had the highest mean fasting glucose level (104.1 mg/dl), followed by enlisted groundcrew (101.8 mg/dl), then officers (100.4 mg/dl). Participants with type B personalities had a higher mean fasting glucose level than did participants with type A personalities (102.9 mg/dl versus 99.6 mg/dl). Participants with a family history of diabetes had a higher mean fasting glucose level (107.1 mg/dl) than did those participants with no family history of diabetes (99.8 mg/dl).

Fasting glucose in its discrete form increased with age ($p=0.001$) and body fat ($p=0.001$). Race ($p=0.040$), personality type ($p=0.001$), and family history of diabetes ($p=0.001$) also were significant in the tests of covariate association. Black participants had a greater percentage of high fasting glucose levels than did non-Black participants (24.2% versus 16.7%). A greater percentage of high fasting glucose values was seen for participants with personality type B (19.4%) versus personality type A (13.6%). Participants with a family history of diabetes had a higher prevalence of high fasting glucose levels (25.2% versus 14.4%).

Two-hour postprandial glucose was analyzed only for nondiabetics. Two-hour postprandial glucose in its continuous form increased with age ($p<0.001$) and body fat ($p<0.001$). Occupation ($p=0.014$), personality type ($p=0.035$), and family history of diabetes ($p=0.003$) also were significant. Enlisted flyers had the highest mean 2-hour postprandial glucose level (109.7 mg/dl), followed by enlisted groundcrew (104.8 mg/dl), then officers (103.5 mg/dl). Participants with type B personalities had a higher mean 2-hour postprandial glucose level than did participants with type A personalities (106.3 mg/dl versus 103.3 mg/dl). Participants with a family history of diabetes had a higher mean 2-hour postprandial glucose level (108.9 mg/dl) than those with no family history of diabetes (104.0 mg/dl).

Tests of covariate association for 2-hour postprandial glucose in its dichotomous form showed age ($p=0.001$), race ($p=0.007$), body fat ($p=0.001$), and family history of diabetes ($p=0.024$) to be significant. The percentage of participants with 2-hour postprandial glucose results classified as impaired increased with age and body fat. Non-Black participants had a higher percentage of impaired values than did Black participants (16.4% versus 5.4%). Participants with a family history of diabetes had a higher prevalence of impaired values than did participants with no family history of diabetes (19.5% versus 14.7%).

The presence of fasting urinary glucose was significantly associated with occupation ($p=0.029$), personality type ($p=0.004$), body fat ($p=0.001$), and family history of diabetes ($p=0.012$). The prevalence of participants with fasting urinary glucose present increased with body fat. Enlisted groundcrew had the highest percentage of positive fasting urinary glucose results (5.2%), followed by enlisted flyers (5.0%), then officers (2.8%). A greater prevalence of participants with fasting urinary glucose present was seen for participants with personality type B (5.2%) versus personality type A (2.6%). Participants with a family history of diabetes had a higher prevalence of positive fasting urinary glucose results than did participants with no family history of diabetes (6.1% versus 3.5%).

Two-hour postprandial urinary glucose was analyzed only for nondiabetics. The presence of 2-hour postprandial urinary glucose was significantly associated with occupation ($p=0.033$). Enlisted flyers had the highest prevalence of positive 2-hour postprandial urinary glucose results (26.7%), followed by enlisted groundcrew (24.9%), then officers (20.1%).

Serum insulin was analyzed only for nondiabetics. Serum insulin in its continuous form increased significantly with age ($p<0.001$) and body fat ($p<0.001$). Occupation ($p=0.001$), personality type ($p=0.006$), and family history of diabetes ($p=0.001$) also were significant. Enlisted flyers had the highest mean serum insulin level (52.55 μIU/ml), followed by enlisted groundcrew (50.58 μIU/ml), then officers (43.67 μIU/ml). Participants with type B personalities had a higher mean serum insulin level than participants with type A personalities (50.42 μIU/ml versus 44.72 μIU/ml). Participants with a family history of diabetes had a higher mean insulin level (54.32 μIU/ml) than those with no family history of diabetes (46.28 μIU/ml).

Serum insulin in its discrete form was significantly associated with age ($p=0.003$), occupation ($p=0.024$), personality type ($p=0.018$), body fat ($p=0.001$), and family history of diabetes ($p=0.001$). Younger participants had a higher percentage of abnormally low and a lower percentage of abnormally high serum insulin levels than did older participants. Officers had the highest percentage of abnormally low serum insulin levels (14.9%) and the lowest percentage of abnormally high serum insulin levels (37.4%). Participants with personality type A had a higher percentage of abnormally low serum insulin levels (14.9%) and a lower percentage of abnormally high serum insulin levels (38.4%) than did participants with personality type B. Obese participants had a lower percentage of abnormally low serum insulin levels (2.5%) than did lean or normal participants (16.4%). Lean or normal participants had a lower percentage of abnormally high serum insulin levels (32.0%) than obese participants (71.0%). Participants with no family history of diabetes had a higher prevalence of abnormally low serum insulin levels (14.2%) than did participants with a history of diabetes (8.5%). The prevalence of abnormally high serum insulin values was greater for participants with a family history of diabetes than for participants with no history of diabetes (49.6% versus 39.4%).

Age and body fat significantly increased with α-1-C hemoglobin in its continuous form ($p<0.001$ for each). Race, occupation, personality type, and family history of diabetes also were significant ($p<0.001$ for each). Black participants had a significantly higher mean α-1-C hemoglobin level than did non-Black participants (7.07 percent versus 6.45 percent). Enlisted flyers had the highest mean α-1-C hemoglobin level (6.61 percent), followed by enlisted groundcrew (6.58 percent), then officers (6.33 percent). Participants with personality type B had a higher mean α-1-C hemoglobin level than did participants with personality type A (6.57 percent versus 6.36 percent). Participants with a family history of diabetes had a higher mean α-1-C hemoglobin level than did participants with no family history of diabetes (6.73 percent versus 6.40 percent).

The discrete form of α-1-C hemoglobin paralleled the continuous analysis. Age ($p=0.001$), race ($p=0.001$), occupation ($p=0.002$), personality type ($p=0.001$), body fat ($p=0.001$), and family history of diabetes ($p=0.001$) were all significantly associated with α-1-C hemoglobin in the tests of covariate association. The covariate categories with the highest mean levels also had the greatest percentage of abnormal high α-1-C hemoglobin levels.

Total testosterone in its continuous form decreased with age and body fat ($p<0.001$ each). Occupation also was significant ($p=0.043$). Officers had the lowest mean total testosterone level (410.7 ng/dl), followed by enlisted groundcrew (429.7 ng/dl), then enlisted flyers (433.4 ng/dl).

Tests of covariate association for total testosterone in its dichotomous form showed body fat to be significant (p=0.001). Obese participants had a higher percentage of low testosterone levels than did lean or normal participants (15.3% versus 4.7%).

Free testosterone in its continuous form decreased with age and body fat (p<0.001 each). Occupation (p<0.001) and personality type (p=0.001) also were significant. Officers had the lowest mean free testosterone level (13.12 pg/ml), followed by enlisted flyers (13.99 pg/ml), then enlisted groundcrew (14.65 pg/ml). Participants with type B personalities had a lower mean free testosterone level than did participants with type A personalities (13.68 pg/ml versus 14.37 pg/ml). Free testosterone in its discrete form decreased significantly with age (p=0.001) and body fat (p=0.002).

Both the continuous and discrete forms of estradiol were significantly associated with race (p=0.008 and p=0.013, respectively). Black participants had a higher mean estradiol level as well as a higher percentage of high estradiol values than non-Blacks. The mean estradiol level was 44.26 pg/ml for Blacks and 40.15 pg/ml for non-Blacks. For Blacks, 37.5 percent had high estradiol levels, whereas 27.0 percent of non-Blacks had high estradiol levels.

LH in both its continuous and discrete forms increased significantly with age (p<0.001 and p=0.001, respectively).

FSH in its continuous form increased significantly with age (p<0.001). Occupation was also significantly associated with FSH (p=0.008). Officers had the highest mean FSH level (6.31 mIU/ml), followed by enlisted flyers (6.00 mIU/ml), then enlisted groundcrew (5.75 mIU/ml).

Similarly, FSH in its dichotomous form was significantly associated with age (p=0.001) and occupation (p=0.001). Older participants had a greater percentage of high FSH values (11.2%) than did younger participants (4.0%). Officers had the highest percentage of high FSH results (10.4%), followed by enlisted flyers (9.2%), then enlisted groundcrew (5.5%).

16.2.2 Exposure Analysis

The following section presents results of the statistical analysis of the dependent variables shown in Table 16-1. Four models were examined for each dependent variable. The analyses of these models are presented below. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7, respectively. These analyses were performed both unadjusted and adjusted for relevant covariates. Model 1 examined the relation between the dependent variable and group (i.e., Ranch Hand or Comparison). In this model, exposure was defined as "yes" for Ranch Hands and "no" for Comparisons without regard to the magnitude of the exposure. As an attempt to quantify exposure, three contrasts of Ranch Hands and Comparisons were performed along with the overall Ranch Hand versus Comparison contrast. These three contrasts compared Ranch Hands and Comparisons within each occupational category (i.e., officers, enlisted flyers, and enlisted groundcrew). As described in previous reports and in Table 2-8, the average levels of exposure to dioxin were highest for enlisted groundcrew, followed by enlisted flyers, then officers.

Model 2 explored the relation between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt. If a participant did not have a 1987 dioxin level, the 1992 level was used to estimate the initial dioxin level. If a participant did not have a 1987 or a 1992 dioxin level, the 1997 level was used to estimate the initial dioxin level. A statistical adjustment for the percentage of body fat at the time of the participant's blood measurement of dioxin was included in this model to account for body-fat-related differences in elimination rate (49).

Model 3 divided the Ranch Hands examined in Model 2 into two categories based on their initial dioxin measures. These two categories are referred to as "low Ranch Hand" and "high Ranch Hand." Two additional categories, Ranch Hands with 1987 serum dioxin levels at or below 10 ppt and Comparisons with 1987 serum dioxin levels at or below 10 ppt, were formed and included in the model. Ranch Hands with 1987 serum dioxin levels at or below 10 ppt are referred to as the "background Ranch Hand" category. Dioxin levels in 1992 were used if the 1987 level was not available, and dioxin levels in 1997 were used if the 1987 and 1992 levels were not available. The four categories—Comparisons, background Ranch Hands, low Ranch Hands, and high Ranch Hands—were used in Model 3 analyses. The relation between the dependent variable in each of the three Ranch Hand categories and the dependent variable in the Comparison category was examined. A fourth contrast, exploring the relation of the dependent variable in the combined low and high Ranch Hand categories relative to Comparisons, also was conducted. This combination is referred to in the tables as the "low plus high Ranch Hand" category. As in Model 2, a statistical adjustment for the percentage of body fat at the time of the participant's blood measurement of dioxin was included in this model.

Model 4 examined the relation between the dependent variable and 1987 lipid-adjusted dioxin levels in all Ranch Hands with a dioxin measurement. If a participant did not have a 1987 dioxin measurement, the 1992 measurement was used to determine the dioxin level. If a participant did not have a 1987 or a 1992 dioxin measurement, the 1997 measurement was used to determine the dioxin level.

16.2.2.1 Medical Records Variables

16.2.2.1.1 Past Thyroid Disease

All unadjusted and adjusted analyses for Models 1 through 4 were nonsignificant (Table 16-3(a–h): p>0.17 for each analysis).

Table 16-3. Analysis of Past Thyroid Disease

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***863***	***65 (7.5)***	***0.89 (0.64,1.22)***	***0.456***
	Comparison	***1,246***	***105 (8.4)***		
Officer	Ranch Hand	338	29 (8.6)	0.91 (0.56,1.48)	0.704
	Comparison	492	46 (9.3)		
Enlisted Flyer	Ranch Hand	150	15 (10.0)	1.37 (0.64,2.94)	0.415
	Comparison	187	14 (7.5)		
Enlisted Groundcrew	Ranch Hand	375	21 (5.6)	0.69 (0.40,1.18)	0.171
	Comparison	567	45 (7.9)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.89 (0.64,1.22)***	***0.459***
Officer	0.91 (0.56,1.48)	0.701
Enlisted Flyer	1.37 (0.64,2.94)	0.419
Enlisted Groundcrew	0.70 (0.41,1.19)	0.189

Table 16-3. Analysis of Past Thyroid Disease (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	12 (7.5)	1.13 (0.88,1.45)	0.360
Medium	160	9 (5.6)		
High	158	14 (8.9)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
477	1.20 (0.88,1.64)	0.245

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,208	102 (8.4)		
Background RH	378	30 (7.9)	0.97 (0.64,1.49)	0.906
Low RH	237	15 (6.3)	0.73 (0.41,1.27)	0.263
High RH	241	20 (8.3)	0.94 (0.57,1.56)	0.825
Low plus High RH	478	35 (7.3)	0.83 (0.55,1.24)	0.362

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 16-3. Analysis of Past Thyroid Disease (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Comparison	1,208		
Background RH	376	0.92 (0.60,1.42)	0.707
Low RH	237	0.70 (0.40,1.22)	0.209
High RH	240	1.07 (0.64,1.81)	0.792
Low plus High RH	477	0.87 (0.57,1.30)	0.490

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**	
1987 Dioxin	**n**	**Number (%) Yes**	**Estimated Relative Risk (95% C.I.)[a]**	**p-Value**
Low	287	25 (8.7)	1.01 (0.85,1.20)	0.892
Medium	285	19 (6.7)		
High	284	21 (7.4)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
853	1.10 (0.89,1.36)	0.358

[a] Relative risk for a twofold increase in 1987 dioxin.

16.2.2.1.2 Composite Diabetes Indicator

The composite diabetes indicator variable was a dichotomous classification of whether a participant was considered diabetic or not. A participant with a verified history of diabetes or a postprandial glucose level of greater than or equal to 200 mg/dl was considered diabetic for these analyses.

The Model 1 unadjusted and adjusted analyses did not show a significant difference in the number of diabetic participants between Ranch Hands and Comparisons across all occupations or within each occupational stratum (Table 16-4(a,b): p>0.49 for each analysis).

Table 16-4. Analysis of Composite Diabetes Indicator

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Diabetic	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***145 (16.9)***	***0.99 (0.79,1.25)***	***0.960***
	Comparison	***1,232***	***209 (17.0)***		
Officer	Ranch Hand	337	52 (15.4)	1.08 (0.73,1.59)	0.709
	Comparison	490	71 (14.5)		
Enlisted Flyer	Ranch Hand	148	27 (18.2)	0.86 (0.50,1.48)	0.583
	Comparison	184	38 (20.7)		
Enlisted Groundcrew	Ranch Hand	374	66 (17.6)	0.98 (0.70,1.38)	0.915
	Comparison	558	100 (17.9)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.04 (0.81,1.33)***	***0.755***
Officer	1.08 (0.72,1.63)	0.711
Enlisted Flyer	0.82 (0.45,1.47)	0.498
Enlisted Groundcrew	1.11 (0.77,1.61)	0.572

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Diabetic	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	157	32 (20.4)	1.11 (0.94,1.32)	0.231
Medium	158	35 (22.2)		
High	160	39 (24.4)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
470	1.36 (1.09,1.69)	0.005

[a] Relative risk for a twofold increase in initial dioxin.

Table 16-4. Analysis of Composite Diabetes Indicator (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Diabetic	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,195	199 (16.7)		
Background RH	379	37 (9.8)	0.67 (0.45,0.98)	0.041
Low RH	235	49 (20.9)	1.27 (0.88,1.84)	0.202
High RH	240	57 (23.8)	1.33 (0.94,1.90)	0.111
Low plus High RH	475	106 (22.3)	1.30 (0.99,1.72)	0.064

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,183		
Background RH	375	0.69 (0.46,1.02)	0.065
Low RH	232	1.22 (0.83,1.79)	0.311
High RH	238	1.47 (1.00,2.17)	0.048
Low plus High RH	470	1.34 (1.00,1.80)	0.049

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Diabetic	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	286	22 (7.7)	1.35 (1.20,1.52)	<0.001
Medium	284	54 (19.0)		
High	284	67 (23.6)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 16-4. Analysis of Composite Diabetes Indicator (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
845	1.43 (1.21,1.68)	<0.001

[a] Relative risk for a twofold increase in 1987 dioxin.

The unadjusted Model 2 analysis did not reveal a significant relation between initial dioxin and the percentage of diabetic participants (Table 16-4(c): p=0.231). After adjusting for covariates, the results became significant (Table 16-4(d): Adj. RR=1.36, p=0.005). The percentages of diabetic participants in the low, medium, and high initial dioxin categories were 20.4, 22.2, and 24.4, respectively.

The unadjusted Model 3 analysis of the composite diabetes indicator revealed significant differences between Ranch Hands in the background dioxin category and Comparisons, as well as between Ranch Hands in the low plus high dioxin category and Comparisons (Table 16-4(e): Est. RR=0.67, p=0.041; Est. RR=1.30, p=0.064, respectively). After adjusting for covariates, three significant contrasts were revealed: Ranch Hands in the background dioxin category versus Comparisons (Table 16-4(f): Adj. RR=0.69, p=0.065), Ranch Hands in the high dioxin category versus Comparisons (Table 16-4(f): Adj. RR=1.47, p=0.048), and Ranch Hands in the low plus high dioxin category versus Comparisons (Table 16-4(f): Adj. RR=1.34, p=0.049). The percentage of diabetic Comparisons was 16.7, versus 9.8 percent for Ranch Hands in the background dioxin category, 23.8 percent of Ranch Hands in the high dioxin category, and 22.3 percent for Ranch Hands in the low plus high dioxin category.

The unadjusted and adjusted Model 4 analyses each revealed a significant positive association between 1987 dioxin and the percentage of diabetic participants (Table 16-4(g,h): Est. RR=1.35, p<0.001; Adj. RR=1.43, p<0.001, respectively). The percentages of diabetic participants in the low, medium, and high 1987 dioxin categories were 7.7, 19.0, and 23.6, respectively.

16.2.2.1.3 Diabetic Severity

The unadjusted Model 1 analysis of diabetic severity revealed marginally significant or significant differences between the percentage of Ranch Hands and Comparisons taking oral hypoglycemics (Table 16-5(a): Est. RR=0.71, p=0.097) and requiring insulin (Table 16-5(a): Est. RR=2.04, p=0.026). The percentage of participants taking oral hypoglycemics was 4.4 for Ranch Hands versus 6.3 for Comparisons. The percentage of participants requiring insulin in the Ranch Hand group was 2.8 versus 1.4 in the Comparison group. Stratifying by occupation revealed a marginally significant difference between the percentage of Ranch Hand and Comparison officers requiring insulin (Table 16-5(a): Est. RR=2.53, p=0.054). For Ranch Hand officers, 3.6 percent required insulin versus 1.4 percent for Comparison officers. After adjusting for covariates, a significant difference in the percentage of Ranch Hands and Comparisons requiring insulin was observed (Table 16-5(b): Adj. RR=2.20, p=0.017). In addition, marginally significant differences were seen between the percentage of Ranch Hands and Comparisons requiring insulin in both the officer stratum and the enlisted groundcrew stratum (Table 16-5(b): Adj. RR=2.39, p=0.074; Adj. RR=2.52, p=0.084, respectively).

The unadjusted Model 2 analysis of diabetic severity did not reveal a significant relation between initial dioxin and the severity of diabetes (Table 16-5(c): p≥0.25 for each contrast). After adjusting for covariates, the percentage of Ranch Hands taking oral hypoglycemic and requiring insulin was associated

significantly with initial dioxin (Table 16-5(d): Adj. RR=1.41, p=0.062 for oral hypoglycemics; Adj. RR=2.47, p=0.001 for requiring insulin). The percentages of Ranch Hands taking oral hypoglycemics in the low, medium, and high initial dioxin categories were 5.1, 6.3, and 8.8, respectively. The percentages of participants requiring insulin in the low, medium, and high initial dioxin categories were 2.5, 3.8, and 3.8, respectively.

The Model 3 unadjusted analysis revealed a significant difference between the percentage of Ranch Hands in the background dioxin category and Comparisons who took oral hypoglycemics to control diabetes (Table 16-5(e): Est. RR=0.27, p=0.006). For Ranch Hands in the background dioxin category, 1.3 percent used oral hypoglycemics versus 6.0 percent of Comparisons. Three Ranch Hand dioxin categories were significantly different from the Comparisons in the percentage of participants requiring insulin: Ranch Hands in the low dioxin category versus Comparisons (Table 16-5(e): Est. RR=2.43, p=0.042), Ranch Hands in the high dioxin category versus Comparisons (Table 16-5(e): Est. RR=2.40, p=0.046), and Ranch Hands in the low plus high dioxin category versus Comparisons (Table 16-5(e): Est. RR=2.41, p=0.013). The percentages of requiring insulin Ranch Hands in the low dioxin category, high dioxin category, and low plus high dioxin category were 3.4, 3.3, and 3.4, respectively, versus 1.4 percent for Comparisons.

The adjusted Model 3 analysis revealed a marginally significant difference between the percentage of Ranch Hands in the high dioxin category and Comparisons who used diet only to control diabetes (Table 16-5(f): Adj. RR=2.32, p=0.089). For Ranch Hands in the high dioxin category, 2.9 percent used diet alone to treat their diabetes versus 1.4 percent of Comparisons. A significant difference between the percentage of Ranch Hands in the background dioxin category and Comparisons who took oral hypoglycemics was observed (Table 16-5(f): Adj. RR=0.28, p=0.008). Three Ranch Hand dioxin categories were significantly different from the Comparisons in the percentage of participants that required insulin: Ranch Hands in the low dioxin category (Table 16-5(f): Adj. RR=2.41, p=0.050), Ranch Hands in the high dioxin category (Table 16-5(f): Adj. RR=3.46, p=0.009), and Ranch Hands in the low plus high dioxin category (Table 16-5(f): Adj. RR=2.90, p=0.004).

The unadjusted Model 4 analysis of diabetic severity revealed a significant positive association between 1987 dioxin and the percentage of diabetics who used no treatment for diabetes (Table 16-5(g): Est. RR=1.28, p=0.010). A positive association between 1987 dioxin and the percentage of diabetics using oral hypoglycemics also was observed (Table 16-5(g): Est. RR=1.58, p<0.001). Adjusting for covariates revealed significant or marginally significant positive associations with 1987 dioxin for all four contrasts: no treatment (Table 16-5(h): Adj. RR=1.23, p=0.097), diet only (Table 16-5(h): Adj. RR=1.49, p=0.048), oral hypoglycemic (Table 16-5(h): Adj. RR=1.85, p<0.001), and requiring insulin (Table 16-5(h): Adj. RR=1.38, p=0.084).

Table 16-5. Analysis of Diabetic Severity

(a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Number (%) Nondiabetic	No Treatment	Diet Only	Oral Hypo-glycemic	Requiring Insulin	Contrast vs. Nondiabetic	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***730 (85.0)***	***49 (5.7)***	***18 (2.1)***	***38 (4.4)***	***24 (2.8)***	***No Treatment***	***1.07 (0.73,1.57)***	***0.721***
	Comparison	***1,232***	***1,054 (85.6)***	***66 (5.4)***	***18 (1.5)***	***77 (6.3)***	***17 (1.4)***	***Diet Only***	***1.44 (0.75,2.79)***	***0.275***
								Oral Hypo-glycemic	***0.71 (0.48,1.06)***	***0.097***
								Requiring Insulin	***2.04 (1.09,3.82)***	***0.026***
Officer	Ranch Hand	337	289 (85.8)	16 (4.7)	8 (2.4)	12 (3.6)	12 (3.6)	No Treatment	0.94 (0.49,1.80)	0.859
	Comparison	490	426 (86.9)	25 (5.1)	6 (1.2)	26 (5.3)	7 (1.4)	Diet Only	1.97 (0.67,5.72)	0.215
								Oral Hypo-glycemic	0.68 (0.34,1.37)	0.281
								Requiring Insulin	2.53 (0.98,6.50)	0.054
Enlisted Flyer	Ranch Hand	148	125 (84.5)	9 (6.1)	2 (1.4)	9 (6.1)	3 (2.0)	No Treatment	0.78 (0.33,1.87)	0.579
	Comparison	184	152 (82.6)	14 (7.6)	2 (1.1)	12 (6.5)	4 (2.2)	Diet Only	1.22 (0.17,8.76)	0.846
								Oral Hypo-glycemic	0.91 (0.37,2.23)	0.840
								Requiring Insulin	0.91 (0.20,4.15)	0.905
Enlisted Groundcrew	Ranch Hand	374	316 (84.5)	24 (6.4)	8 (2.1)	17 (4.5)	9 (2.4)	No Treatment	1.34 (0.76,2.36)	0.314
	Comparison	558	476 (85.3)	27 (4.8)	10 (1.8)	39 (7.0)	6 (1.1)	Diet Only	1.21 (0.47,3.09)	0.697
								Oral Hypo-glycemic	0.66 (0.37,1.18)	0.160
								Requiring Insulin	2.26 (0.80,6.41)	0.125

Table 16-5. Analysis of Diabetic Severity (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	Contrast vs. Nondiabetic	Adj. Relative Risk (95% C.I.)	p-Value
All	***No Treatment***	***1.10 (0.74,1.62)***	***0.642***
	Diet Only	***1.52 (0.78,2.96)***	***0.219***
	Oral Hypoglycemic	***0.73 (0.48,1.11)***	***0.137***
	Requiring Insulin	***2.20 (1.15,4.20)***	***0.017***
Officer	No Treatment	0.96 (0.50,1.86)	0.902
	Diet Only	2.04 (0.69,5.99)	0.195
	Oral Hypoglycemic	0.68 (0.33,1.39)	0.288
	Requiring Insulin	2.39 (0.92,6.20)	0.074
Enlisted Flyer	No Treatment	0.71 (0.29,1.72)	0.445
	Diet Only	1.09 (0.15,7.93)	0.931
	Oral Hypoglycemic	0.75 (0.29,1.91)	0.544
	Requiring Insulin	1.22 (0.24,6.24)	0.811
Enlisted Groundcrew	No Treatment	1.48 (0.83,2.66)	0.185
	Diet Only	1.32 (0.51,3.41)	0.572
	Oral Hypoglycemic	0.76 (0.41,1.41)	0.384
	Requiring Insulin	2.52 (0.88,7.23)	0.084

Table 16-5. Analysis of Diabetic Severity (Continued)

(c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category	n	Initial Dioxin Category Summary Statistics Number (%) Nondiabetic	No Treatment	Diet Only	Oral Hypoglycemic	Requiring Insulin	Analysis Results for Log_2 (Initial Dioxin)[a] Contrast vs. Nondiabetic	Est. Relative Risk (95% C.I.)[b]	p-Value
Low	157	131 (83.4)	11 (7.0)	3 (1.9)	8 (5.1)	4 (2.5)	No Treatment	1.14 (0.87,1.49)	0.332
Medium	158	128 (81.0)	9 (5.7)	5 (3.2)	10 (6.3)	6 (3.8)	Diet Only	1.12 (0.74,1.71)	0.584
High	160	124 (77.5)	12 (7.5)	4 (2.5)	14 (8.8)	6 (3.8)	Oral Hypoglycemic	1.13 (0.87,1.48)	0.358
							Requiring Insulin	1.23 (0.86,1.76)	0.250

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

n	Analysis Results for Log_2 (Initial Dioxin) Contrast vs. Nondiabetic	Adjusted Relative Risk (95% C.I.)[a]	p-Value
470	No Treatment	1.29 (0.93,1.78)	0.121
	Diet Only	1.25 (0.74,2.11)	0.411
	Oral Hypoglycemic	1.41 (0.98,2.01)	0.062
	Requiring Insulin	2.47 (1.43,4.25)	0.001

[a] Relative risk for a twofold increase in initial dioxin.

Table 16-5. Analysis of Diabetic Severity (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED						
		Number (%)				
Dioxin Category	n	Nondiabetic	No Treatment	Diet Only	Oral Hypoglycemic	Requiring Insulin
Comparison	1,195	1,026 (85.9)	63 (5.3)	17 (1.4)	72 (6.0)	17 (1.4)
Background RH	379	344 (90.8)	16 (4.2)	6 (1.6)	5 (1.3)	8 (2.1)
Low RH	235	195 (83.0)	13 (5.5)	5 (2.1)	14 (6.0)	8 (3.4)
High RH	240	188 (78.3)	19 (7.9)	7 (2.9)	18 (7.5)	8 (3.3)
Low plus High RH	475	383 (80.6)	32 (6.7)	12 (2.5)	32 (6.7)	16 (3.4)

	Contrast vs. Nondiabetic							
	No Treatment		Diet Only		Oral Hypoglycemic		Requiring Insulin	
Dioxin Category	Est. Relative Risk (95% C.I.)[ab]	p-Value	Est. Relative Risk (95% C.I.)[ab]	p-Value	Est. Relative Risk (95% C.I.)[ab]	p-Value	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison								
Background RH	0.91 (0.51,1.61)	0.749	1.23 (0.48,3.17)	0.668	0.27 (0.11,0.69)	0.006	1.55 (0.66,3.63)	0.318
Low RH	1.04 (0.55,1.94)	0.912	1.49 (0.54,4.11)	0.437	0.92 (0.49,1.72)	0.795	2.43 (1.03,5.72)	0.042
High RH	1.43 (0.83,2.47)	0.202	2.00 (0.81,4.92)	0.131	1.08 (0.61,1.91)	0.799	2.40 (1.02,5.65)	0.046
Low plus High RH	1.22 (0.77,1.92)	0.394	1.73 (0.81,3.70)	0.156	1.00 (0.63,1.58)	0.988	2.41 (1.20,4.83)	0.013

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 16-5. Analysis of Diabetic Severity (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
		No Treatment vs. Nondiabetic		Diet Only vs. Nondiabetic	
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,183				
Background RH	375	0.92 (0.51,1.65)	0.771	1.24 (0.47,3.30)	0.661
Low RH	232	0.95 (0.50,1.80)	0.878	1.55 (0.55,4.34)	0.408
High RH	238	1.58 (0.89,2.81)	0.122	2.32 (0.88,6.12)	0.089
Low plus High RH	470	1.23 (0.77,1.95)	0.385	1.90 (0.87,4.15)	0.108

		Oral Hypoglycemic vs. Nondiabetic		Requiring Insulin vs. Nondiabetic	
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,183				
Background RH	375	0.28 (0.11,0.71)	0.008	1.42 (0.59,3.45)	0.435
Low RH	232	0.89 (0.46,1.71)	0.726	2.41 (1.00,5.82)	0.050
High RH	238	1.17 (0.63,2.18)	0.624	3.46 (1.36,8.81)	0.009
Low plus High RH	470	1.02 (0.63,1.65)	0.931	2.90 (1.40,5.99)	0.004

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 16-5. Analysis of Diabetic Severity (Continued)

(g) MODEL 4: RANCH HANDS — 1987 DIOXIN — UNADJUSTED

		1987 Dioxin Category Summary Statistics Number (%)					Analysis Results for Log_2 (1987 Dioxin +1)[a]		
Initial Dioxin Category	n	Nondiabetic	No Treatment	Diet Only	Oral Hypoglycemic	Requiring Insulin	Contrast vs. Nondiabetic	Est. Relative Risk (95% C.I.)[a]	p-Value
Low	286	264 (92.3)	11 (3.8)	2 (0.7)	3 (1.1)	6 (2.1)	No Treatment	1.28 (1.06,1.55)	0.010
Medium	284	239 (84.2)	17 (6.0)	8 (2.8)	12 (4.2)	8 (2.8)	Diet Only	1.27 (0.94,1.72)	0.120
High	284	224 (78.9)	20 (7.0)	8 (2.8)	22 (7.7)	10 (3.5)	Oral Hypoglycemic	1.58 (1.28,1.94)	<0.001
							Requiring Insulin	1.15 (0.87,1.50)	0.323

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS — 1987 DIOXIN — ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin + 1)		
n	Contrast vs. Nondiabetic	Adjusted Relative Risk (95% C.I.)[a]	p-Value
845	No Treatment	1.23 (0.96,1.58)	0.097
	Diet Only	1.49 (1.00,2.20)	0.048
	Oral Hypoglycemic	1.85 (1.37,2.49)	<0.001
	Requiring Insulin	1.38 (0.96,2.00)	0.084

[a] Relative risk for a twofold increase in 1987 dioxin.

16.2.2.1.4 Time to Diabetes Onset

The time to diabetes onset from time of duty in SEA did not differ significantly between Ranch Hands and Comparisons in the Model 1 unadjusted and adjusted analyses (Table 16-6(a,b): p≥0.39 for each analysis).

Table 16-6. Analysis of Time to Diabetes Onset (years)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED				
Occupational Category	**Group**	**n**	**Coefficient (Std. Error)[a]**	**p-Value[b]**
All	***Ranch Hand***	***859***	***0.018 (0.035)***	***0.603***
	Comparison	***1,232***		
Officer	Ranch Hand	337	–0.008 (0.077)	0.916
	Comparison	490		
Enlisted Flyer	Ranch Hand	148	0.064 (0.075)	0.390
	Comparison	184		
Enlisted Groundcrew	Ranch Hand	374	0.015 (0.041)	0.715
	Comparison	558		

[a] Coefficient and standard error for group in a survival time analysis model, using a censored Weibull distribution. A negative coefficient implies that the time to diabetes onset is shorter for Ranch Hands than for Comparisons.
[b] P-value based on the group coefficient in a survival time analysis model, using a censored Weibull distribution.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED				
Occupational Category	**Group**	**n**	**Adj. Coefficient (Std. Error)[a]**	**p-Value[b]**
All	***Ranch Hand***	***850***	***0.006 (0.035)***	***0.871***
	Comparison	***1,220***		
Officer	Ranch Hand	335	–0.001 (0.079)	0.993
	Comparison	488		
Enlisted Flyer	Ranch Hand	145	0.066 (0.077)	0.390
	Comparison	178		
Enlisted Groundcrew	Ranch Hand	370	–0.018 (0.043)	0.666
	Comparison	554		

[a] Coefficient and standard error for group in a survival time analysis model, using a censored Weibull distribution. A negative coefficient implies that the time to diabetes onset is shorter for Ranch Hands than for Comparisons.
[b] P-value based on the group coefficient in a survival time analysis model, using a censored Weibull distribution.

Table 16-6. Analysis of Time to Diabetes Onset (years) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED			
Initial Dioxin Category Summary Statistics		Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Slope (Std. Error)[b]	p-Value
Low	157	–0.0214 (0.023)	0.356
Medium	158		
High	160		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Slope and standard error based on time to diabetes onset versus $\log_2$ (initial dioxin) in a survival time analysis model, using a censored Weibull distribution. A negative slope implies that the time to diabetes onset is shorter as initial dioxin increases.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED			
Initial Dioxin Category Summary Statistics		Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Adjusted Slope (Std. Error)[a]	p-Value
Low	156	–0.074 (0.030)	0.013
Medium	154		
High	160		

[a] Slope and standard error based on time to diabetes onset versus $\log_2$ (initial dioxin) in a survival time analysis model, using a censored Weibull distribution. A negative slope implies that the time to diabetes onset is shorter as initial dioxin increases.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED			
Dioxin Category	n	Coefficient (Std. Error)[ab]	p-Value[c]
Comparison	1,195		
Background RH	379	0.143 (0.058)	0.013
Low RH	235	–0.058 (0.051)	0.254
High RH	240	–0.058 (0.048)	0.233
Low plus High RH	475	–0.058 (0.039)	0.134

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Coefficient and standard error for Ranch Hand versus Comparison contrast in a survival time analysis model, using a censored Weibull distribution. A negative coefficient implies that the time to diabetes onset is shorter for the Ranch Hand category than for Comparisons.
[c] P-value based on the Ranch Hand versus Comparison contrast in a survival time analysis model, using a censored Weibull distribution.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 16-6. Analysis of Time to Diabetes Onset (years) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adj. Coefficient (Std. Error)[a]	p-Value[b]
Comparison	1,183		
Background RH	375	0.134 (0.059)	0.024
Low RH	232	–0.065 (0.052)	0.214
High RH	238	–0.085 (0.051)	0.100
Low plus High RH	470	–0.075 (0.040)	0.061

[a] Coefficient and standard error for Ranch Hand versus Comparison contrast in a survival time analysis model, using a censored Weibull distribution. A negative coefficient implies that the time to diabetes onset is shorter for the Ranch Hand category than for Comparisons.
[b] P-value based on the Ranch Hand versus Comparison contrast in a survival time analysis model, using a censored Weibull distribution.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED			
1987 Dioxin Category Summary Statistics		Analysis Results for Log_2 (1987 Dioxin +1)	
1987 Dioxin	n	Slope (Std. Error)[a]	p-Value
Low	286	–0.098 (0.021)	<0.001
Medium	284		
High	284		

[a] Slope and standard error based on time to diabetes onset versus $\log_2$ (1987 dioxin + 1) in a survival time analysis model, using a censored Weibull distribution. A negative slope implies that the time to diabetes onset is shorter as 1987 dioxin increases.

Note: Low = ≤7.9 ppt; Medium = >7.9-19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED			
1987 Dioxin Category Summary Statistics		Analysis Results for Log_2 (1987 Dioxin +1)	
1987 Dioxin	n	Adjusted Slope (Std. Error)[a]	p-Value
Low	282	–0.118 (0.027)	<0.001
Medium	283		
High	280		

[a] Slope and standard error based on time to diabetes onset versus $\log_2$ (1987 dioxin + 1) in a survival time analysis model, using a censored Weibull distribution. A negative slope implies that the time to diabetes onset is shorter as 1987 dioxin increases.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

The Model 2 unadjusted analysis did not reveal a significant relation between initial dioxin and time to diabetes onset (Table 16-6(c): p=0.356). After adjusting for covariates, the results became significant (Table 16-6(d): adjusted slope=–0.074, p=0.013). The time to diabetes onset was shorter for Ranch Hands with higher initial dioxin levels.

The Model 3 unadjusted and adjusted analyses each revealed a significant difference in time to diabetes onset between Ranch Hands in the background dioxin category and Comparisons (Table 16-6(e,f): p=0.013, unadjusted; p=0.024, adjusted). The time to diabetes onset was significantly longer for Ranch Hands in the background dioxin category than for Comparisons. The adjusted Model 3 analysis also revealed two other marginally significant contrasts: Ranch Hands in the high dioxin category versus Comparisons (Table 16-6(f): p=0.100) and Ranch Hands in the low plus high dioxin category versus Comparisons (Table 16-6(f): p=0.061). In each of these two contrasts, the time to diabetes onset from time of duty in SEA was shorter for the Ranch Hand category than for the Comparison category.

The unadjusted and adjusted Model 4 analyses each revealed a significant association between time to diabetes onset and 1987 dioxin (Table 16-6(g,h): slope=–0.098, p<0.001; adjusted slope=–0.118, p<0.001, respectively). In each analysis, the time to diabetes onset was shorter for Ranch Hands with higher 1987 dioxin levels.

16.2.2.2 Physical Examination Variables

16.2.2.2.1 Thyroid Gland

All unadjusted and adjusted analyses in Models 1 through 4 showed no significant associations with dioxin (Table 16-7(a–h): p>0.11 for each analysis).

Table 16-7. Analysis of Thyroid Gland

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***843***	***6 (0.7)***	***0.53 (0.21,1.36)***	***0.171***
	Comparison	***1,203***	***16 (1.3)***		
Officer	Ranch Hand	328	4 (1.2)	0.52 (0.16,1.63)	0.260
	Comparison	470	11 (2.3)		
Enlisted Flyer	Ranch Hand	144	1 (0.7)	1.27 (0.08,20.41)	0.868
	Comparison	182	1 (0.5)		
Enlisted Groundcrew	Ranch Hand	371	1 (0.3)	0.37 (0.04,3.32)	0.374
	Comparison	551	4 (0.7)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.54 (0.21,1.39)***	***0.183***
Officer	0.53 (0.17,1.67)	0.276
Enlisted Flyer	1.23 (0.08,19.88)	0.883
Enlisted Groundcrew	0.38 (0.04,3.39)	0.384

Note: Results are not adjusted for race because of the sparse number of participants with an abnormal thyroid gland.

Table 16-7. Analysis of Thyroid Gland (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	157	1 (0.6)	0.95 (0.32,2.81)	0.923
Medium	158	0 (0.0)		
High	152	1 (0.7)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
466	1.01 (0.32,3.17)	0.981

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race and occupation because of the sparse number of Ranch Hands with an abnormal thyroid gland.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,165	16 (1.4)		
Background RH	369	4 (1.1)	0.82 (0.27,2.47)	0.718
Low RH	233	1 (0.4)	0.31 (0.04,2.32)	0.253
High RH	234	1 (0.4)	0.30 (0.04,2.27)	0.242
Low plus High RH	467	2 (0.4)	0.30 (0.07,1.32)	0.112

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 16-7. Analysis of Thyroid Gland (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,165		
Background RH	367	0.65 (0.21,2.01)	0.457
Low RH	233	0.29 (0.04,2.19)	0.229
High RH	233	0.56 (0.07,4.62)	0.590
Low plus High RH	466	0.40 (0.09,1.81)	0.234

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for race because of the sparse number of participants with an abnormal thyroid gland.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	279	3 (1.1)	0.85 (0.47,1.51)	0.562
Medium	280	2 (0.7)		
High	277	1 (0.4)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
833	1.09 (0.50,2.36)	0.825

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race because of the sparse number of Ranch Hands with an abnormal thyroid gland.

16.2.2.2.2 Testicular Examination

The unadjusted and adjusted Model 1 and 2 analyses of testicular examination were nonsignificant (Table 16-8(a–d): p>0.10 for each analysis).

Table 16-8. Analysis of Testicular Examination

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***861***	***39 (4.5)***	***1.20 (0.78,1.85)***	***0.409***
	Comparison	***1,237***	***47 (3.8)***		
Officer	Ranch Hand	336	16 (4.8)	0.86 (0.45,1.62)	0.635
	Comparison	490	27 (5.5)		
Enlisted Flyer	Ranch Hand	148	9 (6.1)	1.42 (0.54,3.79)	0.478
	Comparison	184	8 (4.3)		
Enlisted Groundcrew	Ranch Hand	377	14 (3.7)	1.77 (0.81,3.87)	0.152
	Comparison	563	12 (2.1)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.20 (0.77,1.87)***	***0.427***
Officer	0.84 (0.44,1.62)	0.611
Enlisted Flyer	1.31 (0.48,3.55)	0.595
Enlisted Groundcrew	1.96 (0.88,4.39)	0.101

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	158	10 (6.3)	0.93 (0.66,1.29)	0.653
Medium	162	8 (4.9)		
High	158	6 (3.8)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
477	1.08 (0.72,1.61)	0.714

[a] Relative risk for a twofold increase in initial dioxin.

Table 16-8. Analysis of Testicular Examination (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,199	47 (3.9)		
Background RH	376	14 (3.7)	0.89 (0.49,1.65)	0.722
Low RH	237	15 (6.3)	1.68 (0.92,3.06)	0.091
High RH	241	9 (3.7)	1.00 (0.48,2.07)	0.994
Low plus High RH	478	24 (5.0)	1.29 (0.77,2.16)	0.333

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,199		
Background RH	374	0.84 (0.45,1.58)	0.594
Low RH	237	1.46 (0.78,2.71)	0.236
High RH	240	1.39 (0.63,3.03)	0.415
Low plus High RH	477	1.42 (0.82,2.45)	0.207

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	284	9 (3.2)	1.01 (0.81,1.26)	0.903
Medium	284	17 (6.0)		
High	286	12 (4.2)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 16-8. Analysis of Testicular Examination (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
851	1.09 (0.82,1.44)	0.545

[a] Relative risk for a twofold increase in 1987 dioxin.

The unadjusted Model 3 analysis revealed a marginally significant difference in the percentage of abnormal testicular examination results between Ranch Hands in the low dioxin category and Comparisons (Table 16-8(e): Est. RR=1.68, p=0.091). The percentage of participants with abnormal testicular examination results for Ranch Hands in the low dioxin category was 6.3 versus 3.9 percent for the Comparisons. After covariate adjustment, the results were not significant (Table 16-8(f): p>0.20 for each contrast).

The unadjusted and adjusted Model 4 analyses of testicular examination were not significant (Table 16-8(g,h): p>0.54 for each analysis).

16.2.2.3 Laboratory Examination Variables

16.2.2.3.1 TSH (Continuous)

The unadjusted Model 1 analysis of TSH in its continuous form did not reveal any significant mean differences between Ranch Hands and Comparisons across all occupations or within each occupational stratum (Table 16-9(a): p≥0.13 for each contrast). The adjusted analysis showed no significant overall group difference between Ranch Hands and Comparisons (Table 16-9(b): p=0.105). Stratifying the adjusted analysis by occupation revealed a marginally significant difference between Ranch Hands and Comparisons in the enlisted groundcrew stratum (Table 16-9(b): difference of adjusted means=0.11 μIU/ml, p=0.088). The adjusted mean TSH level for Ranch Hand enlisted groundcrew was 1.71 μIU/ml versus 1.60 μIU/ml for Comparison enlisted groundcrew.

Table 16-9. Analysis of TSH (μIU/ml) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***841***	***1.88***	***0.08 --***	***0.130***
	Comparison	***1,199***	***1.81***		
Officer	Ranch Hand	326	2.01	0.12 --	0.170
	Comparison	468	1.89		
Enlisted Flyer	Ranch Hand	144	1.72	–0.10 --	0.428
	Comparison	182	1.82		
Enlisted Groundcrew	Ranch Hand	371	1.84	0.11 --	0.139
	Comparison	549	1.73		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 16-9. Analysis of TSH (μIU/ml) (Continuous)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***838***	***1.64***	***0.07 --***	***0.105***
	Comparison	***1,199***	***1.57***		
Officer	Ranch Hand	325	1.69	0.10 --	0.178
	Comparison	468	1.59		
Enlisted Flyer	Ranch Hand	143	1.48	–0.09 --	0.370
	Comparison	182	1.58		
Enlisted Groundcrew	Ranch Hand	370	1.71	0.11 --	0.088
	Comparison	549	1.60		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	157	1.94	1.94	0.002	–0.015 (0.021)	0.475
Medium	158	1.85	1.85			
High	152	1.78	1.78			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of TSH versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	157	1.53	0.071	–0.019 (0.024)	0.433
Medium	157	1.45			
High	152	1.39			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of TSH versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 16-9. Analysis of TSH (µIU/ml) (Continuous)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	**n**	**Mean[a]**	**Adj. Mean[ab]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]**	**p-Value[d]**
Comparison	1,161	1.80	1.80		
Background RH	367	1.90	1.91	0.11 --	0.129
Low RH	233	1.90	1.89	0.09 --	0.273
High RH	234	1.82	1.81	0.01 --	0.942
Low plus High RH	467	1.86	1.85	0.05 --	0.446

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	**n**	**Adj. Mean[a]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]**	**p-Value[c]**
Comparison	1,161	1.57		
Background RH	365	1.64	0.07 --	0.250
Low RH	233	1.64	0.07 --	0.292
High RH	233	1.62	0.05 --	0.454
Low plus High RH	466	1.63	0.06 --	0.237

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 16-9. Analysis of TSH (µIU/ml) (Continuous)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	278	1.88	<0.001	–0.000 (0.015)	0.977
Medium	279	1.98			
High	277	1.77			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of TSH versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	276	1.53	0.046	0.008 (0.017)	0.624
Medium	279	1.62			
High	276	1.48			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of TSH versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Unadjusted and adjusted analyses for Models 2, 3, and 4 showed no significant relations between TSH in its continuous form and dioxin (Table 16-9(c–h): p>0.12 for each analysis).

16.2.2.3.2 TSH (Discrete)

The unadjusted and adjusted Model 1 analyses of TSH in its discrete form did not reveal significant differences across all occupations (Table 16-10(a,b): p≥0.14 for each analysis). After stratifying by occupation, both the unadjusted and adjusted analyses revealed significant differences in the percentage of abnormal high TSH values between Ranch Hand and Comparison enlisted groundcrew (Table 16-10(a,b): Est. RR=2.06, p=0.044; Adj. RR=2.11, p=0.037, respectively). Of the Ranch Hand enlisted groundcrew, 5.1 percent had abnormally high TSH values versus 2.6 percent of the Comparison enlisted groundcrew.

Unadjusted and adjusted analyses in Models 2, 3, and 4 did not show significant associations between dioxin and TSH in its discrete form (Table 16-10(c–h): p>0.12 for each analysis).

Table 16-10. Analysis of TSH (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal Low	Number (%) Normal	Number (%) Abnormal High	Abnormal Low vs. Normal: Est. Relative Risk (95% C.I.)	Abnormal Low vs. Normal: p-Value	Abnormal High vs. Normal: Est. Relative Risk (95% C.I.)	Abnormal High vs. Normal: p-Value
All	***Ranch Hand***	***841***	***10 (1.2)***	***795 (94.5)***	***36 (4.3)***	***1.61 (0.65,3.98)***	***0.301***	***1.41 (0.88,2.25)***	***0.149***
	Comparison	***1,199***	***9 (0.8)***	***1,153 (96.2)***	***37 (3.1)***				
Officer	Ranch Hand	326	4 (1.2)	308 (94.5)	14 (4.3)	2.92 (0.53,16.01)	0.218	1.20 (0.58,2.47)	0.620
	Comparison	468	2 (0.4)	449 (95.9)	17 (3.6)				
Enlisted Flyer	Ranch Hand	144	3 (2.1)	138 (95.8)	3 (2.1)	1.89 (0.31,11.48)	0.488	0.63 (0.15,2.57)	0.519
	Comparison	182	2 (1.1)	174 (95.6)	6 (3.3)				
Enlisted Groundcrew	Ranch Hand	371	3 (0.8)	349 (94.1)	19 (5.1)	0.91 (0.22,3.84)	0.899	2.06 (1.02,4.16)	0.044
	Comparison	549	5 (0.9)	530 (96.5)	14 (2.6)				

(b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Abnormal Low vs. Normal: Adj. Relative Risk (95% C.I.)	Abnormal Low vs. Normal: p-Value	Abnormal High vs. Normal: Adj. Relative Risk (95% C.I.)	Abnormal High vs. Normal: p-Value
All	***1.57 (0.63,3.88)***	***0.332***	***1.42 (0.89,2.28)***	***0.140***
Officer	2.78 (0.50,15.33)	0.241	1.18 (0.57,2.44)	0.648
Enlisted Flyer	2.01 (0.33,12.28)	0.448	0.63 (0.15,2.55)	0.513
Enlisted Groundcrew	0.88 (0.21,3.71)	0.859	2.11 (1.04,4.28)	0.037

Table 16-10. Analysis of TSH (Discrete) (Continued)

(c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED								
Initial Dioxin Category Summary Statistics					Analysis Results for Log_2 (Initial Dioxin)[a]			
		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Initial Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
Low	157	1 (0.6)	150 (95.5)	6 (3.8)	1.40 (0.73,2.71)	0.311	1.27 (0.89,1.79)	0.183
Medium	158	0 (0.0)	154 (97.5)	4 (2.5)				
High	152	3 (2.0)	142 (93.4)	7 (4.6)				

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Initial Dioxin)			
	Abnormal Low vs. Normal		Abnormal High vs. Normal	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
467	1.62 (0.82,3.20)	0.161	1.29 (0.90,1.85)	0.169

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for occupation and personality type because of the sparse number of Ranch Hands with an abnormally low TSH level.

Table 16-10. Analysis of TSH (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED								
		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[a,b]	p-Value	Est. Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,161	9 (0.8)	1,116 (96.1)	36 (3.1)				
Background RH	367	6 (1.6)	344 (93.7)	17 (4.6)	2.27 (0.80,6.50)	0.125	1.46 (0.80,2.64)	0.214
Low RH	233	1 (0.4)	225 (96.6)	7 (3.0)	0.54 (0.07,4.31)	0.564	0.97 (0.43,2.22)	0.951
High RH	234	3 (1.3)	221 (94.4)	10 (4.3)	1.60 (0.43,6.02)	0.485	1.47 (0.72,3.02)	0.294
Low plus High RH	467	4 (0.9)	446 (95.5)	17 (3.6)	0.93 (0.25,3.48)	0.919	1.20 (0.66,2.17)	0.553

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 16-10. Analysis of TSH (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
		Abnormal Low vs. Normal		Abnormal High vs. Normal	
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,161				
Background RH	365	2.33 (0.79,6.87)	0.125	1.43 (0.78,2.62)	0.244
Low RH	233	0.52 (0.06,4.15)	0.536	0.98 (0.43,2.24)	0.963
High RH	233	1.51 (0.39,5.91)	0.550	1.58 (0.74,3.35)	0.236
Low plus High RH	466	0.89 (0.24,3.33)	0.858	1.24 (0.68,2.28)	0.481

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS — 1987 DIOXIN — UNADJUSTED								
	1987 Dioxin Category Summary Statistics				Analysis Results for Log_2 (1987 Dioxin + 1)			
		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
1987 Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[a]	p-Value	Est. Relative Risk (95% C.I.)[a]	p-Value
Low	278	4 (1.4)	260 (93.5)	14 (5.0)	0.97 (0.63,1.48)	0.881	0.98 (0.78,1.24)	0.894
Medium	279	3 (1.1)	266 (95.3)	10 (3.6)				
High	277	3 (1.1)	264 (95.3)	10 (3.6)				

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 16-10. Analysis of TSH (Discrete) (Continued)

(h) MODEL 4: RANCH HANDS — 1987 DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (1987 Dioxin + 1)			
	Abnormal Low vs. Normal		Abnormal High vs. Normal	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
831	1.08 (0.64,1.83)	0.767	0.97 (0.74,1.27)	0.832

[a] Relative risk for a twofold increase in 1987 dioxin.

16.2.2.3.3 Thyroxine (Continuous)

The unadjusted and adjusted Models 1 and 2 analyses of thyroxine in its continuous form were not significant (Table 16-11(a,b): p>0.12 for each analysis).

Table 16-11. Analysis of Thyroxine (μg/dl) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	**Group**	**n**	**Mean[a]**	**Difference of Means (95% C.I.)[b]**	**p-Value[c]**
All	***Ranch Hand***	***841***	***7.07***	***0.03 --***	***0.601***
	Comparison	***1,199***	***7.04***		
Officer	Ranch Hand	326	6.76	–0.08 --	0.373
	Comparison	468	6.84		
Enlisted Flyer	Ranch Hand	144	7.28	0.03 --	0.818
	Comparison	182	7.24		
Enlisted Groundcrew	Ranch Hand	371	7.27	0.12 --	0.154
	Comparison	549	7.15		

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	**Group**	**n**	**Adjusted Mean[a]**	**Difference of Adj. Means (95% C.I.)[b]**	**p-Value[c]**
All	***Ranch Hand***	***838***	***6.96***	***0.03 --***	***0.565***
	Comparison	***1,199***	***6.93***		
Officer	Ranch Hand	325	6.58	–0.08 --	0.370
	Comparison	468	6.66		
Enlisted Flyer	Ranch Hand	143	7.12	0.04 --	0.774
	Comparison	182	7.08		
Enlisted Groundcrew	Ranch Hand	370	7.19	0.13 --	0.129
	Comparison	549	7.06		

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

Table 16-11. Analysis of Thyroxine (μg/dl) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	157	7.11	7.12	0.012	0.010 (0.008)	0.250
Medium	158	7.15	7.16			
High	152	7.28	7.26			

[a] Transformed from square root scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on square root of thyroxine versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	157	6.99	0.045	–0.004 (0.010)	0.682
Medium	157	6.89			
High	152	6.89			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of thyroxine versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,161	7.04	7.04		
Background RH	367	6.95	6.95	–0.09 --	0.221
Low RH	233	7.13	7.13	0.09 --	0.344
High RH	234	7.23	7.23	0.19 --	0.053
Low plus High RH	467	7.18	7.18	0.14 --	0.059

[a] Transformed from square root scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[d] P-value is based on difference of means on square root scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 16-11. Analysis of Thyroxine (μg/dl) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,161	6.93		
Background RH	365	6.93	0.00 --	0.969
Low RH	233	7.02	0.09 --	0.344
High RH	233	6.98	0.05 --	0.646
Low plus High RH	466	7.00	0.07 --	0.357

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	278	6.95	0.008	0.015 (0.006)	0.009
Medium	279	7.03			
High	277	7.25			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of thyroxine versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	276	6.92	0.047	–0.001 (0.007)	0.862
Medium	279	6.91			
High	276	6.91			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of thyroxine versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

The unadjusted Model 3 analysis of thyroxine in its continuous form revealed two marginally significant contrasts: Ranch Hands in the high dioxin category versus Comparisons and Ranch Hands in the low plus high dioxin category versus Comparisons (Table 16-11(e): difference of means=0.19 μg/dl, p=0.053; difference of means=0.14 μg/dl, p=0.059, respectively). The adjusted analysis did not reveal any significant contrasts (Table 16-11(f): p>0.34 for each contrast).

The Model 4 unadjusted analysis revealed a significant positive association between thyroxine and 1987 dioxin (Table 16-11(g): adjusted slope=0.015, p=0.009). After covariate adjustment, the results became nonsignificant (Table 16-11(h): p=0.862)

16.2.2.3.4 Thyroxine (Discrete)

All unadjusted and adjusted analyses for Models 1 through 4 showed no significant relations between dioxin and thyroxine in its discrete form (Table 16-12(a–h): p>0.14 for each analysis).

Table 16-12. Analysis of Thyroxine (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Low	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***841***	***23 (2.7)***	***1.03 (0.60,1.77)***	***0.928***
	Comparison	***1,199***	***32 (2.7)***		
Officer	Ranch Hand	326	13 (4.0)	1.17 (0.56,2.47)	0.674
	Comparison	468	16 (3.4)		
Enlisted Flyer	Ranch Hand	144	3 (2.1)	1.27 (0.25,6.39)	0.772
	Comparison	182	3 (1.6)		
Enlisted Groundcrew	Ranch Hand	371	7 (1.9)	0.79 (0.31,2.01)	0.624
	Comparison	549	13 (2.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.04 (0.61,1.80)***	***0.875***
Officer	1.21 (0.57,2.55)	0.622
Enlisted Flyer	1.24 (0.25,6.24)	0.796
Enlisted Groundcrew	0.80 (0.32,2.02)	0.636

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Low	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	157	3 (1.9)	1.22 (0.79,1.89)	0.375
Medium	158	1 (0.6)		
High	152	6 (3.9)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 16-12. Analysis of Thyroxine (Discrete) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
466	1.51 (0.87,2.62)	0.143

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race because of the sparse number of Ranch Hands with a low thyroxine level.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Low	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,161	31 (2.7)		
Background RH	367	13 (3.5)	1.40 (0.72,2.71)	0.325
Low RH	233	3 (1.3)	0.47 (0.14,1.55)	0.215
High RH	234	7 (3.0)	1.08 (0.47,2.49)	0.858
Low plus High RH	467	10 (2.1)	0.71 (0.33,1.54)	0.390

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,161		
Background RH	365	1.23 (0.63,2.42)	0.545
Low RH	233	0.45 (0.14,1.49)	0.192
High RH	233	1.53 (0.62,3.73)	0.354
Low plus High RH	466	0.83 (0.38,1.82)	0.641

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 16-12. Analysis of Thyroxine (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Low	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	278	8 (2.9)	0.97 (0.73,1.29)	0.825
Medium	279	8 (2.9)		
High	277	7 (2.5)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
831	1.14 (0.79,1.64)	0.487

[a] Relative risk for a twofold increase in 1987 dioxin.

16.2.2.3.5 Anti-Thyroid Antibodies

All unadjusted and adjusted analyses for Models 1 through 4 were nonsignificant (Table 16-13(a–h): p>0.43 for each analysis).

Table 16-13. Analysis of Anti-Thyroid Antibodies

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Present	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***841***	***5 (0.6)***	***1.02 (0.32,3.22)***	***0.975***
	Comparison	***1,199***	***7 (0.6)***		
Officer	Ranch Hand	326	2 (0.6)	0.72 (0.13,3.93)	0.701
	Comparison	468	4 (0.9)		
Enlisted Flyer	Ranch Hand	144	2 (1.4)	2.55 (0.23,28.40)	0.447
	Comparison	182	1 (0.5)		
Enlisted Groundcrew	Ranch Hand	371	1 (0.3)	0.74 (0.07,8.18)	0.805
	Comparison	549	2 (0.4)		

Table 16-13. Analysis of Anti-Thyroid Antibodies (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.01 (0.32,3.21)***	***0.981***
Officer	0.73 (0.13,4.02)	0.717
Enlisted Flyer	2.62 (0.24,29.23)	0.434
Enlisted Groundcrew	0.73 (0.07,8.06)	0.796

Note: Results are not adjusted for race because of the sparse number of participants with anti-thyroid antibodies present.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Present	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	157	0 (0.0)	0.93 (0.30,2.89)	0.905
Medium	158	2 (1.3)		
High	152	0 (0.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
466	1.01 (0.31,3.23)	0.990

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race and occupation because of the sparse number of Ranch Hands with anti-thyroid antibodies present.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Present	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,161	7 (0.6)		
Background RH	367	3 (0.8)	1.20 (0.30,4.69)	0.798
Low RH	233	1 (0.4)	0.73 (0.09,5.96)	0.768
High RH	234	1 (0.4)	0.80 (0.10,6.56)	0.834
Low plus High RH	467	2 (0.4)	0.76 (0.16,3.70)	0.736

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 16-13. Analysis of Anti-Thyroid Antibodies (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,161		
Background RH	365	1.07 (0.27,4.26)	0.921
Low RH	233	0.73 (0.09,5.99)	0.765
High RH	233	1.07 (0.12,9.66)	0.951
Low plus High RH	466	0.88 (0.17,4.46)	0.879

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for race because of the sparse number of participants with anti-thyroid antibodies present.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Present	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	278	2 (0.7)	0.82 (0.43,1.55)	0.535
Medium	279	2 (0.7)		
High	277	1 (0.4)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
831	0.86 (0.41,1.80)	0.689

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race because of the sparse number of Ranch Hands with anti-thyroid antibodies present.

16.2.2.3.6 Fasting Glucose (Continuous)

The unadjusted and adjusted Model 1 analyses did not reveal a significant difference in mean fasting glucose levels between all Ranch Hands and Comparisons or after stratifying by occupation (Table 16-14(a,b): p>0.38 for each analysis).

Fasting glucose in its continuous form was not significantly associated with initial dioxin in the unadjusted Model 2 analysis (Table 16-14(c): p=0.174). After adjusting for covariates, the results became significant (Table 16-14(d): adjusted slope=0.023, p=0.014). The adjusted mean fasting glucose levels in the low, medium, and high initial dioxin categories were 104.5 mg/dl, 109.2 mg/dl, and 109.5 mg/dl, respectively.

The unadjusted and adjusted Model 3 analyses of fasting glucose showed no significant mean differences between any of the Ranch Hand dioxin categories and Comparisons (Table 16-14(e,f): p>0.10 for each contrast).

Table 16-14. Analysis of Fasting Glucose (mg/dl) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***868***	***101.4***	***–0.3 --***	***0.745***
	Comparison	***1,250***	***101.8***		
Officer	Ranch Hand	339	101.1	1.1 --	0.468
	Comparison	494	100.0		
Enlisted Flyer	Ranch Hand	151	103.2	–1.7 --	0.507
	Comparison	187	104.9		
Enlisted Groundcrew	Ranch Hand	378	101.0	–1.3 --	0.388
	Comparison	569	102.3		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***859***	***103.7***	***0.0 --***	***0.970***
	Comparison	***1,238***	***103.8***		
Officer	Ranch Hand	337	101.9	0.9 --	0.550
	Comparison	492	101.0		
Enlisted Flyer	Ranch Hand	148	104.1	–1.6 --	0.516
	Comparison	181	105.7		
Enlisted Groundcrew	Ranch Hand	374	104.7	–0.3 --	0.819
	Comparison	565	105.1		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 16-14. Analysis of Fasting Glucose (mg/dl) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	159	101.4	102.2	0.102	0.011 (0.008)	0.174
Medium	161	104.5	104.7			
High	160	104.9	103.9			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of fasting glucose versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	158	104.5	0.160	0.023 (0.009)	0.014
Medium	157	109.2			
High	160	109.5			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of fasting glucose versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,212	101.7	101.6		
Background RH	381	98.4	100.3	–1.3 --	0.298
Low RH	238	101.4	100.8	–0.8 --	0.618
High RH	242	105.8	103.9	2.3 --	0.121
Low plus High RH	480	103.6	102.4	0.8 --	0.485

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 16-14. Analysis of Fasting Glucose (mg/dl) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,200	103.8		
Background RH	377	102.8	–1.0 --	0.418
Low RH	235	102.9	–0.9 --	0.551
High RH	240	106.3	2.5 --	0.106
Low plus High RH	475	104.6	0.8 --	0.482

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	288	97.8	0.019	0.020 (0.005)	<0.001
Medium	286	101.6			
High	287	104.6			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of fasting glucose versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	284	101.0	0.082	0.018 (0.006)	0.002
Medium	285	102.7			
High	283	107.2			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of fasting glucose versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Both the unadjusted and adjusted Model 4 analyses showed significant positive associations between fasting glucose in its continuous form and 1987 dioxin (Table 16-14(g,h): slope=0.020, p<0.001, for the

unadjusted analysis; adjusted slope=0.018, p=0.002, for the adjusted analysis). The adjusted mean fasting glucose values in the low, medium, and high 1987 dioxin categories were 101.0 mg/dl, 102.7 mg/dl, and 107.2 mg/dl, respectively.

16.2.2.3.7 Fasting Glucose (Discrete)

The percentage of participants with high fasting glucose levels did not significantly differ between Ranch Hands and Comparisons across all occupations or within each occupational stratum in the Model 1 analysis (Table 16-15(a,b): p>0.52 for each analysis).

Table 16-15. Analysis of Fasting Glucose (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	**Group**	**n**	**Number (%) High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***868***	***152 (17.5)***	***1.04 (0.83,1.31)***	***0.741***
	Comparison	***1,250***	***212 (17.0)***		
Officer	Ranch Hand	339	56 (16.5)	1.11 (0.76,1.61)	0.603
	Comparison	494	75 (15.2)		
Enlisted Flyer	Ranch Hand	151	29 (19.2)	1.00 (0.58,1.72)	0.991
	Comparison	187	36 (19.3)		
Enlisted Groundcrew	Ranch Hand	378	67 (17.7)	1.00 (0.71,1.40)	0.992
	Comparison	569	101 (17.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	**Adjusted Relative Risk (95% C.I.)**	**p-Value**
All	***1.07 (0.84,1.37)***	***0.562***
Officer	1.11 (0.75,1.64)	0.611
Enlisted Flyer	0.90 (0.50,1.60)	0.712
Enlisted Groundcrew	1.12 (0.78,1.61)	0.526

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Number (%) High**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	159	29 (18.2)	1.13 (0.95,1.34)	0.172
Medium	161	35 (21.7)		
High	160	38 (23.8)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 16-15. Analysis of Fasting Glucose (Discrete) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
475	1.31 (1.06,1.62)	0.013

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,212	203 (16.7)		
Background RH	381	48 (12.6)	0.89 (0.63,1.26)	0.517
Low RH	238	44 (18.5)	1.07 (0.73,1.56)	0.721
High RH	242	58 (24.0)	1.35 (0.95,1.91)	0.097
Low plus High RH	480	102 (21.3)	1.20 (0.91,1.59)	0.200

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,200		
Background RH	377	0.91 (0.63,1.31)	0.609
Low RH	235	1.03 (0.70,1.53)	0.877
High RH	240	1.44 (0.99,2.11)	0.056
Low plus High RH	475	1.22 (0.91,1.64)	0.178

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 16-15. Analysis of Fasting Glucose (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	34 (11.8)	1.25 (1.11,1.41)	<0.001
Medium	286	51 (17.8)		
High	287	65 (22.6)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
852	1.25 (1.08,1.46)	0.003

[a] Relative risk for a twofold increase in 1987 dioxin.

The unadjusted Model 2 analysis did not show a significant relation between initial dioxin and the percentage of participants with high fasting glucose levels (Table 16-15(c): p=0.172). After adjusting for covariates, the results became significant (Table 16-15(b): Adj. RR=1.31, p=0.013). The percentages of participants with high fasting glucose values in the low, medium, and high initial dioxin categories were 18.2, 21.7, and 23.8, respectively.

Both the unadjusted and adjusted Model 3 analyses revealed a marginally significant difference in the percentage of high fasting glucose levels between Ranch Hands in the high dioxin category and Comparisons (Table 16-15(e,f): Est. RR=1.35, p=0.097; Adj. RR=1.44, p=0.056, respectively). The percentage of abnormal fasting glucose values for Ranch Hands in the high dioxin category was 24.0 versus 16.7 percent for Comparisons.

The unadjusted and adjusted Model 4 analyses each revealed significant positive associations between high fasting glucose levels and 1987 dioxin (Table 16-15(g,h): Est. RR=1.25, p<0.001; Adj. RR=1.25, p=0.003, respectively). The percentages of participants with high fasting glucose values in the low, medium, and high 1987 dioxin categories were 11.8, 17.8, and 22.6, respectively.

16.2.2.3.8 2-Hour Postprandial Glucose (Continuous)

The unadjusted and adjusted Model 1 analyses of 2-hour postprandial glucose in its continuous form did not show a significant difference between all Ranch Hands and Comparisons (Table 16-16(a,b): p>0.70 for each analysis). Stratifying by occupation revealed significant differences between Ranch Hand and Comparison officers in both the unadjusted and adjusted analyses (Table 16-16(a,b): difference of means=4.3 mg/dl, p=0.053, for the unadjusted analysis; difference of adjusted means=3.5 mg/dl, p=0.086, for the adjusted analysis). The adjusted mean 2-hour postprandial glucose level for Ranch Hand officers was 103.0 mg/dl versus 99.5 mg/dl for Comparison officers.

Table 16-16. Analysis of 2-Hour Postprandial Glucose (mg/dl) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***714***	***105.2***	***0.3 --***	***0.818***
	Comparison	***1,023***	***104.9***		
Officer	Ranch Hand	285	106.1	4.3 --	0.053
	Comparison	419	101.8		
Enlisted Flyer	Ranch Hand	121	107.8	–3.5 --	0.342
	Comparison	146	111.3		
Enlisted Groundcrew	Ranch Hand	308	103.4	–2.3 --	0.274
	Comparison	458	105.8		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***705***	***105.5***	***0.5 --***	***0.702***
	Comparison	***1,014***	***105.0***		
Officer	Ranch Hand	283	103.0	3.5 --	0.086
	Comparison	418	99.5		
Enlisted Flyer	Ranch Hand	118	106.4	–2.9 --	0.405
	Comparison	142	109.3		
Enlisted Groundcrew	Ranch Hand	304	106.0	–1.2 --	0.563
	Comparison	454	107.2		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	125	107.4	108.3	0.076	–0.010 (0.011)	0.363
Medium	123	105.9	106.2			
High	121	107.4	106.2			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of 2-hour postprandial glucose versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 16-16. Analysis of 2-Hour Postprandial Glucose (mg/dl) (Continuous) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	124	108.1	0.139	0.003 (0.013)	0.832
Medium	119	106.7			
High	121	110.3			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of 2-hour postprandial glucose versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	996	104.9	104.7		
Background RH	342	103.6	105.3	0.6 --	0.718
Low RH	186	107.3	107.1	2.4 --	0.296
High RH	183	106.5	104.5	–0.2 --	0.942
Low plus High RH	369	106.9	105.8	1.1 --	0.521

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 16-16. Analysis of 2-Hour Postprandial Glucose (mg/dl) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	**n**	**Adj. Mean[a]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]**	**p-Value[c]**
Comparison	987	105.1		
Background RH	338	106.1	1.0 --	0.585
Low RH	183	106.1	1.0 --	0.655
High RH	181	104.6	–0.5 --	0.804
Low plus High RH	364	105.4	0.3 --	0.900

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin +1)**		
1987 Dioxin	**n**	**Mean[a]**	**R^2**	**Slope (Std. Error)[b]**	**p-Value**
Low	264	103.7	0.003	0.011 (0.007)	0.115
Medium	230	106.0			
High	217	106.5			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of 2-hour postprandial glucose versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**		
1987 Dioxin	**n**	**Adj. Mean[a]**	**R^2**	**Adjusted Slope (Std. Error)[b]**	**p-Value**
Low	260	105.1	0.137	0.002 (0.008)	0.850
Medium	229	103.7			
High	213	105.3			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of 2-hour postprandial glucose versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

The unadjusted and adjusted analyses of 2-hour postprandial glucose in Models 2 through 4 were nonsignificant (Table 16-16(c–h): p>0.11 for each analysis).

16.2.2.3.9 2-Hour Postprandial Glucose (Discrete)

The percentage of participants with impaired 2-hour postprandial glucose levels did not significantly differ between Ranch Hands and Comparisons across all occupations (Table 16-17(a,b): p>0.91 for both unadjusted and adjusted analyses). Stratifying the unadjusted analysis by occupation revealed a marginally significant difference between Ranch Hand and Comparison officers (Table 16-17(a): Est. RR=1.51, p=0.052). The percentage of 2-hour postprandial glucose values classified as impaired for Ranch Hand officers was 18.2 versus 12.9 percent for Comparison officers. No significant contrasts were revealed after stratifying the adjusted analysis by occupation (Table 16-17(b): p≥0.11 for each contrast).

Table 16-17. Analysis of 2-Hour Postprandial Glucose (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Impaired	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***714***	***113 (15.8)***	***1.01 (0.77,1.31)***	***0.960***
	Comparison	***1,023***	***161 (15.7)***		
Officer	Ranch Hand	285	52 (18.2)	1.51 (1.00,2.28)	0.052
	Comparison	419	54 (12.9)		
Enlisted Flyer	Ranch Hand	121	22 (18.2)	0.82 (0.45,1.52)	0.534
	Comparison	146	31 (21.2)		
Enlisted Groundcrew	Ranch Hand	308	39 (12.7)	0.73 (0.48,1.11)	0.136
	Comparison	458	76 (16.6)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.98 (0.75,1.30)***	***0.912***
Officer	1.42 (0.92,2.20)	0.110
Enlisted Flyer	0.81 (0.43,1.54)	0.526
Enlisted Groundcrew	0.75 (0.48,1.16)	0.191

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Impaired	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	125	23 (18.4)	0.88 (0.71,1.10)	0.267
Medium	123	23 (18.7)		
High	121	20 (16.5)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 16-17. Analysis of 2-Hour Postprandial Glucose (Discrete) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
364	0.99 (0.76,1.29)	0.940

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Impaired	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	996	155 (15.6)		
Background RH	342	47 (13.7)	0.98 (0.68,1.40)	0.906
Low RH	186	35 (18.8)	1.27 (0.84,1.92)	0.260
High RH	183	31 (16.9)	1.00 (0.65,1.54)	0.999
Low plus High RH	369	66 (17.9)	1.13 (0.82,1.56)	0.468

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	987		
Background RH	338	0.94 (0.64,1.37)	0.729
Low RH	183	1.12 (0.73,1.72)	0.616
High RH	181	1.01 (0.64,1.60)	0.960
Low plus High RH	364	1.06 (0.76,1.49)	0.722

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 16-17. Analysis of 2-Hour Postprandial Glucose (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Impaired	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	264	38 (14.4)	1.06 (0.92,1.22)	0.394
Medium	230	40 (17.4)		
High	217	35 (16.1)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
702	1.10 (0.91,1.33)	0.332

[a] Relative risk for a twofold increase in 1987 dioxin.

All unadjusted and adjusted Models 2 through 4 analyses were nonsignificant (Table 16-17(c–h): p>0.26 for each analysis).

16.2.2.3.10 Fasting Urinary Glucose

The unadjusted and adjusted Models 1 through 3 analyses of fasting urinary glucose were nonsignificant (Table 16-18(a–f): p>0.12 for each analysis).

Table 16-18. Analysis of Fasting Urinary Glucose

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Present	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***868***	***35 (4.0)***	***0.93 (0.60,1.44)***	***0.745***
	Comparison	***1,250***	***54 (4.3)***		
Officer	Ranch Hand	339	11 (3.2)	1.35 (0.59,3.09)	0.482
	Comparison	494	12 (2.4)		
Enlisted Flyer	Ranch Hand	151	8 (5.3)	1.11 (0.42,2.94)	0.839
	Comparison	187	9 (4.8)		
Enlisted Groundcrew	Ranch Hand	378	16 (4.2)	0.72 (0.39,1.32)	0.288
	Comparison	569	33 (5.8)		

Table 16-18. Analysis of Fasting Urinary Glucose (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.98 (0.63,1.52)***	***0.924***
Officer	1.40 (0.61,3.22)	0.432
Enlisted Flyer	1.13 (0.41,3.11)	0.816
Enlisted Groundcrew	0.77 (0.42,1.43)	0.412

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Present	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	159	5 (3.1)	1.19 (0.90,1.57)	0.220
Medium	161	13 (8.1)		
High	160	9 (5.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
475	1.27 (0.90,1.79)	0.173

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Present	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,212	51 (4.2)		
Background RH	381	7 (1.8)	0.53 (0.24,1.19)	0.124
Low RH	238	9 (3.8)	0.81 (0.38,1.70)	0.571
High RH	242	18 (7.4)	1.51 (0.85,2.69)	0.160
Low plus High RH	480	27 (5.6)	1.11 (0.66,1.85)	0.696

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 16-18. Analysis of Fasting Urinary Glucose (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,200		
Background RH	377	0.63 (0.27,1.43)	0.265
Low RH	235	0.92 (0.43,1.97)	0.827
High RH	240	1.33 (0.71,2.49)	0.369
Low plus High RH	475	1.11 (0.65,1.89)	0.704

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Present	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	3 (1.0)	1.38 (1.12,1.71)	0.004
Medium	286	11 (3.8)		
High	287	20 (7.0)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
852	1.47 (1.11,1.94)	0.006

[a] Relative risk for a twofold increase in 1987 dioxin.

Both the unadjusted and adjusted Model 4 analyses revealed significant positive relations between fasting urinary glucose and 1987 dioxin (Table 16-18(g,h): Est. RR=1.38, p=0.004; Adj. RR=1.47, p=0.006, respectively). The percentages of participants with fasting urinary glucose in the low, medium, and high 1987 dioxin categories were 1.0, 3.8, and 7.0, respectively.

16.2.2.3.11 2-Hour Postprandial Urinary Glucose

The unadjusted Model 1 analysis of 2-hour postprandial urinary glucose did not reveal a significant overall group difference between Ranch Hands and Comparisons (Table 16-19(a): p=0.122). Stratifying the unadjusted analysis by occupation revealed a significant difference between Ranch Hand and Comparison officers (Table 16-19(a): Est. RR=1.49, p=0.034). The prevalence of 2-hour postprandial

urinary glucose was greater for Ranch Hand officers (24.0%) than for Comparison officers (17.5%). The adjusted Model 1 analysis revealed a significant difference between Ranch Hands and Comparisons across all occupations and within the officer stratum (Table 16-19(b): Adj. RR=1.22, p=0.094; Adj. RR=1.47, p=0.044, respectively). The presence of 2-hour postprandial urinary glucose for Ranch Hands was 25.1 percent versus 21.9 percent for Comparisons. For the officers, 24.0 percent of the Ranch Hands had 2-hour postprandial urinary glucose present versus 17.5 percent of the Comparisons.

Table 16-19. Analysis of 2-Hour Postprandial Urinary Glucose

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Present	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***712***	***179 (25.1)***	***1.19 (0.95,1.50)***	***0.122***
	Comparison	***1,021***	***224 (21.9)***		
Officer	Ranch Hand	283	68 (24.0)	1.49 (1.03,2.17)	0.034
	Comparison	418	73 (17.5)		
Enlisted Flyer	Ranch Hand	121	28 (23.1)	0.71 (0.41,1.24)	0.233
	Comparison	145	43 (29.7)		
Enlisted Groundcrew	Ranch Hand	308	83 (26.9)	1.20 (0.86,1.67)	0.291
	Comparison	458	108 (23.6)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.22 (0.97,1.53)***	***0.094***
Officer	1.47 (1.01,2.14)	0.044
Enlisted Flyer	0.73 (0.42,1.28)	0.276
Enlisted Groundcrew	1.26 (0.90,1.76)	0.180

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Present	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	124	34 (27.4)	0.94 (0.78,1.14)	0.535
Medium	123	30 (24.4)		
High	121	30 (24.8)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 16-19. Analysis of 2-Hour Postprandial Urinary Glucose (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
363	0.94 (0.75,1.17)	0.585

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Present	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	994	214 (21.5)		
Background RH	341	85 (24.9)	1.20 (0.90,1.60)	0.222
Low RH	185	52 (28.1)	1.43 (1.00,2.03)	0.050
High RH	183	42 (23.0)	1.10 (0.75,1.60)	0.636
Low plus High RH	368	94 (25.5)	1.25 (0.95,1.65)	0.118

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	985		
Background RH	337	1.32 (0.98,1.78)	0.072
Low RH	182	1.41 (0.98,2.02)	0.064
High RH	181	0.97 (0.66,1.44)	0.885
Low plus High RH	363	1.17 (0.88,1.56)	0.283

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 16-19. Analysis of 2-Hour Postprandial Urinary Glucose (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Present	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	264	70 (26.5)	0.97 (0.86,1.10)	0.664
Medium	228	54 (23.7)		
High	217	55 (25.3)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
700	0.90 (0.78,1.03)	0.129

[a] Relative risk for a twofold increase in 1987 dioxin.

Both the unadjusted and adjusted Model 2 analyses were nonsignificant (Table 16-19(c,d): p>0.53 for each analysis).

A significant difference between Ranch Hands in the low dioxin category and Comparisons was seen in the unadjusted Model 3 analysis of 2-hour postprandial urinary glucose (Table 16-19(e): Est. RR=1.43, p=0.050). After adjusting for covariates, two marginally significant contrasts were seen: Ranch Hands in the background dioxin category versus Comparisons (Table 16-19(f): Adj. RR=1.32, p=0.072) and Ranch Hands in the low dioxin category versus Comparisons (Table 16-19(f): Adj. RR=1.41, p=0.064). The presence of 2-hour postprandial urinary glucose for Ranch Hands in the background dioxin category, Ranch Hands in the low dioxin category, and Comparisons was 24.9 percent, 28.1 percent, and 21.5 percent, respectively.

The unadjusted and adjusted Model 4 analyses did not reveal a significant association between 2-hour postprandial urinary glucose and 1987 dioxin (Table 16-19(g,h): p>0.12 for each analysis).

16.2.2.3.12 Serum Insulin (Continuous)

The unadjusted and adjusted Models 1 and 2 analyses of serum insulin in its continuous form were nonsignificant (Table 16-20(a–d): p≥0.17 for each analysis).

The unadjusted Model 3 analysis revealed a significant difference in mean serum insulin levels between Ranch Hands in the low plus high dioxin category and Comparisons (Table 16-20(e): difference of means=5.00 µIU/ml, p=0.046). The mean serum insulin level for Ranch Hands in the low plus high dioxin category was 52.35 µIU/ml versus 47.35 µIU/ml for Comparisons. After adjusting for covariates, the results became nonsignificant (Table 16-20(f): p>0.19 for each contrast).

Table 16-20. Analysis of Serum Insulin (μIU/ml) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***714***	***47.95***	***0.03 --***	***0.990***
	Comparison	***1,023***	***47.92***		
Officer	Ranch Hand	285	45.60	3.20 --	0.283
	Comparison	419	42.40		
Enlisted Flyer	Ranch Hand	121	49.81	–5.11 --	0.369
	Comparison	146	54.92		
Enlisted Groundcrew	Ranch Hand	308	49.49	–1.84 --	0.574
	Comparison	458	51.33		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***705***	***49.07***	***1.09 --***	***0.562***
	Comparison	***1,014***	***47.99***		
Officer	Ranch Hand	283	43.72	2.40 --	0.353
	Comparison	418	41.32		
Enlisted Flyer	Ranch Hand	118	49.21	–2.99 --	0.548
	Comparison	142	52.20		
Enlisted Groundcrew	Ranch Hand	304	53.35	1.05 --	0.735
	Comparison	454	52.31		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	125	52.55	54.14	0.092	0.020 (0.036)	0.571
Medium	123	52.18	52.70			
High	121	59.81	57.42			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of serum insulin versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 16-20. Analysis of Serum Insulin (μIU/ml) (Continuous) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	124	57.88	0.195	0.054 (0.040)	0.170
Medium	119	56.68			
High	121	67.03			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of serum insulin versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	996	47.73	47.35		
Background RH	342	42.18	45.29	–2.06 --	0.393
Low RH	186	52.51	51.97	4.62 --	0.157
High RH	183	57.01	52.74	5.39 --	0.105
Low plus High RH	369	54.70	52.35	5.00 --	0.046

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 16-20. Analysis of Serum Insulin (µIU/ml) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	987	47.57		
Background RH	338	47.31	–0.26 --	0.914
Low RH	183	49.87	2.30 --	0.455
High RH	181	51.51	3.94 --	0.226
Low plus High RH	364	50.68	3.11 --	0.195

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	264	41.18	0.025	0.100 (0.023)	<0.001
Medium	230	49.71			
High	217	56.76			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of serum insulin versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	260	46.56	0.235	0.026 (0.025)	0.305
Medium	229	47.08			
High	213	53.05			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of serum insulin versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

The unadjusted Model 4 analysis revealed a significant relation between serum insulin in its continuous form and 1987 dioxin (Table 16-20(g): slope=0.100, p<0.001). The mean serum insulin levels in the low, medium, and high 1987 dioxin categories were 41.18 µIU/ml, 49.71 µIU/ml, and 56.76 µIU/ml, respectively. After adjustment for covariates, the association was nonsignificant (Table 16-20(h): p=0.305).

16.2.2.3.13 Serum Insulin (Discrete)

Unadjusted and adjusted analyses in Models 1 and 2 did not show significant associations between dioxin and serum insulin in its discrete form (Table 16-21(a–d): p>0.14 for each analysis).

The unadjusted Model 3 analysis revealed a marginally significant difference between the percentage of Ranch Hands in the high dioxin category and Comparisons with abnormally low serum insulin levels (Table 16-21(e): Est. RR=0.58, p=0.082). The adjusted Model 3 analysis of abnormally low serum insulin levels revealed two marginally significant contrasts: Ranch Hands in the high dioxin category versus Comparisons (Table 16-21(f): Adj. RR=0.55, p=0.081) and Ranch Hands in the low plus high dioxin category versus Comparisons (Table 16-21(f): Adj. RR=0.68, p=0.093). The percentages of abnormally low serum insulin values for Ranch Hands in the high dioxin category, Ranch Hands in the low plus high dioxin category, and Comparisons were 7.1, 8.9, and 13.2, respectively.

The unadjusted Model 4 analysis revealed a significant association between 1987 dioxin and both abnormally low serum insulin levels (Table 16-21(g): Est. RR=0.83, p=0.050) and abnormally high serum insulin levels (Table 16-21(g): Est. RR=1.16, p=0.008). The percentage of participants with abnormally low serum insulin levels decreased with 1987 dioxin while the percentage of participants with abnormally high serum insulin levels increased with 1987 dioxin. The percentages of participants with abnormally low serum insulin levels in the low, medium, and high 1987 dioxin categories were 15.2, 11.7, and 7.8, respectively. The percentages of participants with abnormally high serum insulin levels in the low, medium, and high 1987 dioxin categories were 34.1, 41.7, and 49.8, respectively. Model 4 adjusted analyses showed no significant association between abnormal serum insulin levels and 1987 dioxin (p>0.58 for both contrasts).

Table 16-21. Analysis of Serum Insulin (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED										
			Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal		
Occupational Category	Group	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)	p-Value	Est. Relative Risk (95% C.I.)	p-Value	
All	***Ranch Hand***	***714***	***86 (12.0)***	***334 (46.8)***	***294 (41.2)***	***0.85 (0.62,1.15)***	***0.278***	***0.92 (0.75,1.13)***	***0.443***	
	Comparison	***1,023***	***138 (13.5)***	***453 (44.3)***	***432 (42.2)***					
Officer	Ranch Hand	285	36 (12.6)	137 (48.1)	112 (39.3)	0.76 (0.48,1.20)	0.235	1.08 (0.78,1.49)	0.655	
	Comparison	419	69 (16.5)	199 (47.5)	151 (36.0)					
Enlisted Flyer	Ranch Hand	121	15 (12.4)	56 (46.3)	50 (41.3)	1.11 (0.49,2.51)	0.803	0.70 (0.42,1.17)	0.173	
	Comparison	146	14 (9.6)	58 (39.7)	74 (50.7)					
Enlisted Groundcrew	Ranch Hand	308	35 (11.4)	141 (45.8)	132 (42.9)	0.88 (0.55,1.42)	0.613	0.89 (0.65,1.21)	0.442	
	Comparison	458	55 (12.0)	196 (42.8)	207 (45.2)					

(b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED				
	Abnormal Low vs. Normal		Abnormal High vs. Normal	
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Adj. Relative Risk (95% C.I.)	p-Value
All	***0.79 (0.58,1.08)***	***0.143***	***0.96 (0.77,1.21)***	***0.749***
Officer	0.76 (0.48,1.22)	0.256	1.08 (0.75,1.53)	0.688
Enlisted Flyer	0.83 (0.35,1.95)	0.671	0.72 (0.41,1.27)	0.257
Enlisted Groundcrew	0.81 (0.50,1.33)	0.412	0.97 (0.69,1.36)	0.870

Table 16-21. Analysis of Serum Insulin (Discrete) (Continued)

(c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category	Initial Dioxin Category Summary Statistics				Analysis Results for Log₂ (Initial Dioxin)[a]			
		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
Low	125	12 (9.6)	61 (48.8)	52 (41.6)	0.96 (0.70,1.32)	0.815	1.07 (0.90,1.28)	0.447
Medium	123	13 (10.6)	51 (41.5)	59 (48.0)				
High	121	8 (6.6)	52 (43.0)	61 (50.4)				

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

	Analysis Results for Log₂ (Initial Dioxin)			
	Abnormal Low vs. Normal		Abnormal High vs. Normal	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
364	0.97 (0.65,1.47)	0.901	1.15 (0.93,1.43)	0.182

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race because of the sparse number of Ranch Hands with an abnormally low serum insulin level.

Table 16-21. Analysis of Serum Insulin (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED								
		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[ab]	p-Value	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	996	131 (13.2)	447 (44.9)	418 (42.0)				
Background RH	342	51 (14.9)	169 (49.4)	122 (35.7)	0.96 (0.66,1.39)	0.820	0.91 (0.69,1.20)	0.507
Low RH	186	20 (10.8)	81 (43.5)	85 (45.7)	0.84 (0.50,1.43)	0.527	1.14 (0.81,1.61)	0.460
High RH	183	13 (7.1)	83 (45.4)	87 (47.5)	0.58 (0.31,1.07)	0.082	0.99 (0.70,1.40)	0.968
Low plus High RH	369	33 (8.9)	164 (44.4)	172 (46.6)	0.70 (0.45,1.07)	0.102	1.06 (0.82,1.39)	0.643

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 16-21. Analysis of Serum Insulin (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
		Abnormal Low vs. Normal		Abnormal High vs. Normal	
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
Comparison	987				
Background RH	338	0.90 (0.61,1.31)	0.573	0.99 (0.74,1.34)	0.971
Low RH	183	0.82 (0.47,1.44)	0.496	1.00 (0.70,1.44)	0.994
High RH	181	0.55 (0.29,1.08)	0.081	0.94 (0.65,1.37)	0.759
Low plus High RH	364	0.68 (0.43,1.07)	0.093	0.97 (0.74,1.28)	0.843

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS — 1987 DIOXIN — UNADJUSTED								
	1987 Dioxin Category Summary Statistics				Analysis Results for Log_2 (1987 Dioxin + 1)			
		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
1987 Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[a]	p-Value	Est. Relative Risk (95% C.I.)[a]	p-Value
Low	264	40 (15.2)	134 (50.8)	90 (34.1)	0.83 (0.69,1.00)	0.050	1.16 (1.04,1.30)	0.008
Medium	230	27 (11.7)	107 (46.5)	96 (41.7)				
High	217	17 (7.8)	92 (42.4)	108 (49.8)				

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 16-21. Analysis of Serum Insulin (Discrete) (Continued)

(h) MODEL 4: RANCH HANDS — 1987 DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (1987 Dioxin + 1)			
	Abnormal Low vs. Normal		Abnormal High vs. Normal	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
702	0.94 (0.76,1.17)	0.589	1.03 (0.89,1.19)	0.685

[a] Relative risk for a twofold increase in 1987 dioxin.

16.2.2.3.14 *α-1-C Hemoglobin (Continuous)*

The unadjusted and adjusted Model 1 analyses did not reveal a significant difference in mean α-1-C hemoglobin levels between all Ranch Hands and Comparisons or after stratifying by occupation (Table 16-22(a,b): $p \geq 0.28$ for each analysis).

Table 16-22. Analysis of α-1-C Hemoglobin (percent) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***868***	***6.48***	***–0.01 --***	***0.919***
	Comparison	***1,250***	***6.49***		
Officer	Ranch Hand	339	6.37	0.07 --	0.387
	Comparison	494	6.31		
Enlisted Flyer	Ranch Hand	151	6.53	–0.14 --	0.280
	Comparison	187	6.67		
Enlisted Groundcrew	Ranch Hand	378	6.57	–0.03 --	0.714
	Comparison	569	6.59		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***859***	***6.77***	***0.01 --***	***0.882***
	Comparison	***1,238***	***6.76***		
Officer	Ranch Hand	337	6.61	0.06 --	0.427
	Comparison	492	6.55		
Enlisted Flyer	Ranch Hand	148	6.74	–0.14 --	0.284
	Comparison	181	6.88		
Enlisted Groundcrew	Ranch Hand	374	6.91	0.01 --	0.905
	Comparison	565	6.90		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 16-22. Analysis of α-1-C Hemoglobin (percent) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	159	6.43	6.47	0.107	0.017 (0.006)	0.009
Medium	161	6.70	6.71			
High	160	6.77	6.72			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of α-1-C hemoglobin versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	158	6.68	0.163	0.024 (0.007)	0.001
Medium	157	7.01			
High	160	7.05			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of α-1-C hemoglobin versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,212	6.49	6.48		
Background RH	381	6.29	6.38	–0.10 --	0.116
Low RH	238	6.47	6.44	–0.04 --	0.588
High RH	242	6.79	6.70	0.22 --	0.005
Low plus High RH	480	6.63	6.57	0.09 --	0.138

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 16-22. Analysis of α-1-C Hemoglobin (percent) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,200	6.78		
Background RH	377	6.72	–0.06 --	0.412
Low RH	235	6.70	–0.08 --	0.330
High RH	240	6.97	0.19 --	0.022
Low plus High RH	475	6.83	0.05 --	0.363

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	288	6.24	0.033	0.021 (0.004)	<0.001
Medium	286	6.46			
High	287	6.74			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of α-1-C hemoglobin versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	284	6.63	0.119	0.016 (0.005)	<0.001
Medium	285	6.68			
High	283	7.02			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of α-1-C hemoglobin versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Both the unadjusted and adjusted Model 2 analyses revealed significant relations between α-1-C hemoglobin and initial dioxin (Table 16-22(c,d): slope=0.017, p=0.009, for the unadjusted analysis;

adjusted slope=0.024, p=0.001, for the adjusted analysis). The adjusted mean α-1-C hemoglobin levels in the low, medium, and high initial dioxin categories were 6.68, 7.01, and 7.05 percent, respectively.

The unadjusted and adjusted Model 3 analyses each revealed a significant difference between Ranch Hands in the high dioxin category and Comparisons (Table 16-22(e,f): difference of means=0.22 percent, p=0.005, for the unadjusted analysis; difference of adjusted means=0.19 percent, p=0.022, for the adjusted analysis). The adjusted mean α-1-C hemoglobin level for Ranch Hands in the high dioxin category was 6.97 percent versus 6.78 percent for the Comparisons.

A significant relation was seen between α-1-C hemoglobin in its continuous form and 1987 dioxin in each of the unadjusted and adjusted Model 4 analyses (Table 16-22(g,h): slope=0.021, p<0.001; adjusted slope=0.016, p<0.001, respectively). The adjusted mean α-1-C hemoglobin levels in the low, medium, and high initial dioxin categories were 6.63 percent, 6.68 percent, and 7.02 percent, respectively.

16.2.2.3.15 α-1-C Hemoglobin (Discrete)

The unadjusted Model 1 analysis of α-1-C hemoglobin in its discrete from did not reveal any significant differences between Ranch Hands and Comparisons across all occupations or within each occupational stratum (Table 16-23(a): p≥0.25 for each contrast). The adjusted analysis did not reveal a significant overall group difference between Ranch Hands and Comparisons (Table 16-23(b): p=0.373). After stratifying by occupation, a marginally significant difference was seen between Ranch Hand and Comparison enlisted groundcrew (Table 16-23(b): Adj. RR=1.43, p=0.087). The percentage of Ranch Hand enlisted groundcrew with high α-1-C hemoglobin values was 13.8 percent versus 11.2 percent for Comparison enlisted groundcrew.

Table 16-23. Analysis of α-1-C Hemoglobin (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	**Group**	**n**	**Number (%) High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***868***	***97 (11.2)***	***1.08 (0.82,1.43)***	***0.571***
	Comparison	***1,250***	***130 (10.4)***		
Officer	Ranch Hand	339	28 (8.3)	1.11 (0.67,1.85)	0.684
	Comparison	494	37 (7.5)		
Enlisted Flyer	Ranch Hand	151	17 (11.3)	0.69 (0.36,1.31)	0.259
	Comparison	187	29 (15.5)		
Enlisted Groundcrew	Ranch Hand	378	52 (13.8)	1.26 (0.85,1.86)	0.250
	Comparison	569	64 (11.2)		

Table 16-23. Analysis of α-1-C Hemoglobin (Discrete) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.14 (0.85,1.53)***	***0.373***
Officer	1.13 (0.67,1.90)	0.652
Enlisted Flyer	0.65 (0.33,1.28)	0.210
Enlisted Groundcrew	1.43 (0.95,2.16)	0.087

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	159	16 (10.1)	1.28 (1.05,1.56)	0.013
Medium	161	23 (14.3)		
High	160	31 (19.4)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
475	1.53 (1.19,1.96)	0.001

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,212	125 (10.3)		
Background RH	381	25 (6.6)	0.75 (0.47,1.18)	0.210
Low RH	238	25 (10.5)	0.95 (0.60,1.53)	0.841
High RH	242	45 (18.6)	1.73 (1.17,2.55)	0.006
Low plus High RH	480	70 (14.6)	1.29 (0.92,1.80)	0.138

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 16-23. Analysis of α-1-C Hemoglobin (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,200		
Background RH	377	0.84 (0.53,1.35)	0.474
Low RH	235	0.94 (0.58,1.52)	0.799
High RH	240	1.76 (1.16,2.67)	0.008
Low plus High RH	475	1.29 (0.91,1.82)	0.148

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	16 (5.6)	1.39 (1.21,1.60)	<0.001
Medium	286	28 (9.8)		
High	287	51 (17.8)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
852	1.37 (1.15,1.64)	<0.001

[a] Relative risk for a twofold increase in 1987 dioxin.

The unadjusted and adjusted Model 2 analyses each revealed significant associations between initial dioxin and α-1-C hemoglobin in its dichotomous form (Table 16-23(c,d): Est. RR=1.28, p=0.013; Adj. RR=1.53, p=0.001, respectively). The percentages of Ranch Hands with high α-1-C hemoglobin values in the low, medium, and high initial dioxin categories were 10.1, 14.3, and 19.4, respectively.

The Model 3 unadjusted and adjusted analyses each revealed a significant difference in the percentage of high α-1-C hemoglobin values between Ranch Hands in the high dioxin category and Comparisons (Table 16-23(e,f): Est. RR=1.73, p=0.006; Adj. RR=1.76, p=0.008, respectively). The percentage of high α-1-C hemoglobin values for Ranch Hands in the high dioxin category was 18.6 versus 10.3 percent for Comparisons.

A significant relation was seen between α-1-C hemoglobin and 1987 dioxin in each of the Model 4 unadjusted and adjusted analyses (Table 16-23(g,h): Est. RR=1.39, $p<0.001$; Adj. RR=1.37, $p<0.001$, respectively). The percentages of participants with high α-1-C hemoglobin values in the low, medium, and high 1987 dioxin categories were 5.6, 9.8, and 17.8, respectively.

16.2.2.3.16 Total Testosterone (Continuous)

The unadjusted and adjusted Model 1 analyses did not reveal any significant differences in mean total testosterone levels between Ranch Hands and Comparisons across all occupations or within each occupational stratum (Table 16-24(a,b): $p>0.57$ for each contrast).

Table 16-24. Analysis of Total Testosterone (ng/dl) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***850***	***423.1***	***0.5 --***	***0.945***
	Comparison	***1,227***	***422.6***		
Officer	Ranch Hand	330	406.9	–6.4 --	0.606
	Comparison	485	413.4		
Enlisted Flyer	Ranch Hand	146	439.6	11.2 --	0.577
	Comparison	182	428.4		
Enlisted Groundcrew	Ranch Hand	374	431.2	2.5 --	0.835
	Comparison	560	428.7		

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***847***	***422.3***	***–1.1 --***	***0.883***
	Comparison	***1,227***	***423.4***		
Officer	Ranch Hand	329	412.5	–2.2 --	0.848
	Comparison	485	414.7		
Enlisted Flyer	Ranch Hand	145	439.6	9.2 --	0.618
	Comparison	182	430.4		
Enlisted Groundcrew	Ranch Hand	373	418.5	–3.7 --	0.733
	Comparison	560	422.2		

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

Table 16-24. Analysis of Total Testosterone (ng/dl) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	156	404.1	397.7	0.118	0.287 (0.144)	0.047
Medium	160	392.3	392.0			
High	156	421.1	428.0			

[a] Transformed from square root scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on square root of total testosterone versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	156	415.1	0.206	–0.015 (0.161)	0.927
Medium	159	395.2			
High	156	404.7			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of total testosterone versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,189	422.0	423.0		
Background RH	372	448.1	429.8	6.8 --	0.499
Low RH	234	399.1	404.6	–18.4 --	0.118
High RH	238	412.1	429.4	6.4 --	0.592
Low plus High RH	472	405.6	417.0	–6.0 --	0.508

[a] Transformed from square root scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[d] P-value is based on difference of means on square root scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 16-24. Analysis of Total Testosterone (ng/dl) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	**n**	**Adj. Mean[a]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]**	**p-Value[c]**
Comparison	1,189	422.9		
Background RH	370	434.4	11.5 --	0.248
Low RH	234	414.5	–8.4 --	0.470
High RH	237	416.8	–6.1 --	0.613
Low plus High RH	471	415.7	–7.2 --	0.420

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	**n**	**Mean[a]**	**R^2**	**Slope (Std. Error)[b]**	**p-Value**
Low	281	455.3	0.010	–0.296 (0.101)	0.003
Medium	281	408.2			
High	282	409.7			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of total testosterone versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	**n**	**Adj. Mean[a]**	**R^2**	**Adjusted Slope (Std. Error)[b]**	**p-Value**
Low	279	439.1	0.193	–0.149 (0.109)	0.172
Medium	281	418.6			
High	281	409.3			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of total testosterone versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

The unadjusted Model 2 analysis revealed a significant relation between initial dioxin and total testosterone in its continuous form (Table 16-24(c): slope=0.287, p=0.047). After adjusting for covariates, the results became nonsignificant (Table 16-24(d): p=0.927).

The unadjusted and adjusted Model 3 analyses of total testosterone showed no significant mean differences between any of the Ranch Hand dioxin categories and the Comparison group (Table 16-24(e,f): p>0.11 for each contrast).

A significant relation between 1987 dioxin and total testosterone was revealed in the unadjusted Model 4 analysis (Table 16-24(g): slope=–0.296, p=0.003). After covariate adjustment, the results became nonsignificant (Table 16-24(h): p=0.172).

16.2.2.3.17 Total Testosterone (Discrete)

The unadjusted and adjusted Models 1 and 2 analyses of total testosterone in its dichotomous form were not significant (Table 16-25(a–d): p>0.30 for each analysis).

Table 16-25. Analysis of Total Testosterone (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Low	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***850***	***72 (8.5)***	***1.17 (0.85,1.61)***	***0.344***
	Comparison	***1,227***	***90 (7.3)***		
Officer	Ranch Hand	330	29 (8.8)	1.28 (0.76,2.14)	0.352
	Comparison	485	34 (7.0)		
Enlisted Flyer	Ranch Hand	146	12 (8.2)	1.39 (0.60,3.25)	0.445
	Comparison	182	11 (6.0)		
Enlisted Groundcrew	Ranch Hand	374	31 (8.3)	1.03 (0.64,1.67)	0.890
	Comparison	560	45 (8.0)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.16 (0.83,1.63)***	***0.378***
Officer	1.22 (0.71,2.07)	0.475
Enlisted Flyer	1.21 (0.50,2.96)	0.673
Enlisted Groundcrew	1.11 (0.67,1.83)	0.688

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Low	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	156	13 (8.3)	1.00 (0.80,1.26)	0.973
Medium	160	19 (11.9)		
High	156	16 (10.3)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 16-25. Analysis of Total Testosterone (Discrete) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
471	1.16 (0.87,1.55)	0.307

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Low	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,189	88 (7.4)		
Background RH	372	23 (6.2)	1.04 (0.64,1.69)	0.878
Low RH	234	20 (8.6)	1.08 (0.64,1.84)	0.767
High RH	238	28 (11.8)	1.40 (0.88,2.25)	0.156
Low plus High RH	472	48 (10.2)	1.23 (0.84,1.82)	0.285

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,189		
Background RH	370	0.98 (0.59,1.62)	0.934
Low RH	234	0.95 (0.55,1.62)	0.841
High RH	237	1.55 (0.94,2.55)	0.085
Low plus High RH	471	1.21 (0.82,1.80)	0.340

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 16-25. Analysis of Total Testosterone (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Low	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	281	17 (6.0)	1.22 (1.05,1.43)	0.013
Medium	281	21 (7.5)		
High	282	33 (11.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
Analysis Results for Log_2 (1987 Dioxin + 1)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
841	1.20 (0.96,1.49)	0.106

[a] Relative risk for a twofold increase in 1987 dioxin.

The unadjusted Model 3 analysis did not reveal any significant differences between any of the Ranch Hand dioxin categories and the Comparison group (Table 16-25(e): p>0.15 for each contrast). Adjusting for covariates revealed a marginally significant difference in the percentage of low total testosterone values between Ranch Hands in the high dioxin category and Comparisons (Table 16-25(f): Adj. RR=1.55, p=0.085). The percentage of low total testosterone values for Ranch Hands in the high dioxin category was 11.8 versus 7.4 percent for Comparisons.

The unadjusted Model 4 analysis revealed a significant relation between 1987 dioxin and total testosterone in its discrete form (Table 16-25(g): Est. RR=1.22, p=0.013). After adjusting for covariates, the results became nonsignificant (Table 16-25(h): p=0.106).

16.2.2.3.18 Free Testosterone (Continuous)

The unadjusted and adjusted Model 1 analyses did not reveal a significant difference in mean free testosterone levels between all Ranch Hands and Comparisons or after stratifying by occupation (Table 16-26(a,b): p>0.20 for each analysis).

Table 16-26. Analysis of Free Testosterone (pg/ml) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***850***	***13.96***	***0.04 --***	***0.852***
	Comparison	***1,227***	***13.92***		
Officer	Ranch Hand	330	12.91	–0.36 --	0.269
	Comparison	485	13.26		
Enlisted Flyer	Ranch Hand	146	14.03	0.08 --	0.878
	Comparison	182	13.95		
Enlisted Groundcrew	Ranch Hand	374	14.89	0.40 --	0.209
	Comparison	560	14.49		

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***847***	***13.80***	***0.01 --***	***0.941***
	Comparison	***1,227***	***13.79***		
Officer	Ranch Hand	329	13.39	–0.21 --	0.464
	Comparison	485	13.61		
Enlisted Flyer	Ranch Hand	145	14.23	0.13 --	0.783
	Comparison	182	14.10		
Enlisted Groundcrew	Ranch Hand	373	13.81	0.17 --	0.528
	Comparison	560	13.64		

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	156	13.08	12.94	0.084	0.066 (0.022)	0.003
Medium	160	13.69	13.68			
High	156	14.59	14.75			

[a] Transformed from square root scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on square root of free testosterone versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 16-26. Analysis of Free Testosterone (pg/ml) (Continuous) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	156	13.42	0.240	–0.008 (0.024)	0.742
Medium	159	13.61			
High	156	13.61			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of free testosterone versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,189	13.93	13.95		
Background RH	372	14.24	13.85	–0.10 --	0.703
Low RH	234	13.11	13.23	–0.72 --	0.022
High RH	238	14.46	14.85	0.90 --	0.006
Low plus High RH	472	13.78	14.03	0.08 --	0.745

[a] Transformed from square root scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[d] P-value is based on difference of means on square root scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,189	13.80		
Background RH	370	13.98	0.18 --	0.459
Low RH	234	13.50	–0.30 --	0.315
High RH	237	13.94	0.14 --	0.643
Low plus High RH	471	13.72	–0.08 --	0.735

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 16-26. Analysis of Free Testosterone (pg/ml) (Continuous) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	281	14.56	0.001	–0.010 (0.015)	0.489
Medium	281	13.17			
High	282	14.23			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of free testosterone versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	279	14.49	0.234	–0.029 (0.016)	0.066
Medium	281	13.65			
High	281	13.66			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of free testosterone versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

A significant association was seen between free testosterone and initial dioxin in the unadjusted Model 2 analysis (Table 16-26(c): slope=0.066, p=0.003). The adjusted analysis results were nonsignificant (Table 16-26(d): p=0.742).

The unadjusted Model 3 analysis of free testosterone in its continuous form revealed two significant contrasts: Ranch Hands in the low dioxin category versus Comparisons and Ranch Hands in the high dioxin category versus Comparisons (Table 16-26(e): difference of means=–0.72 pg/ml, p=0.022; difference of means=0.90 pg/ml, p=0.006, respectively). The adjusted analysis did not reveal any significant contrasts (Table 16-26(f): p>0.31 for each contrast).

The unadjusted Model 4 analysis did not reveal any significant relation between 1987 dioxin and free testosterone in its continuous form (Table 16-26(g): p=0.489). After covariate adjustment, a marginally significant inverse relation between 1987 dioxin and mean free testosterone level was seen (Table 16-26(h): adjusted slope=–0.029, p=0.066). The adjusted mean free testosterone levels in the low, medium, and high 1987 dioxin categories were 14.49 pg/ml, 13.65 pg/ml, and 13.66 pg/ml, respectively.

16.2.2.3.19 Free Testosterone (Discrete)

The unadjusted and adjusted Model 1 analyses did not reveal a significant overall group difference between Ranch Hands and Comparisons (Table 16-27(a,b): p>0.81 for both analyses). In each of the unadjusted and adjusted analyses, stratifying by occupation revealed a marginally significant difference between Ranch Hands and Comparisons in the enlisted flyer stratum (Table 16-27(a,b): Est. RR=7.76,

p=0.059; Adj. RR=6.41, p=0.091, respectively). The percentage of low free testosterone values for the Ranch Hand enlisted flyers was 4.1 versus 0.5 percent for Comparison enlisted flyers.

Table 16-27. Analysis of Free Testosterone (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Low	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***850***	***15 (1.8)***	***1.08 (0.55,2.13)***	***0.815***
	Comparison	***1,227***	***20 (1.6)***		
Officer	Ranch Hand	330	7 (2.1)	1.03 (0.39,2.73)	0.954
	Comparison	485	10 (2.1)		
Enlisted Flyer	Ranch Hand	146	6 (4.1)	7.76 (0.92,65.18)	0.059
	Comparison	182	1 (0.5)		
Enlisted Groundcrew	Ranch Hand	374	2 (0.5)	0.33 (0.07,1.53)	0.157
	Comparison	560	9 (1.6)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.09 (0.54,2.19)***	***0.812***
Officer	1.06 (0.39,2.90)	0.911
Enlisted Flyer	6.41 (0.74,55.13)	0.091
Enlisted Groundcrew	0.37 (0.08,1.76)	0.210

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Low	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	156	5 (3.2)	0.46 (0.21,0.98)	0.019
Medium	160	4 (2.5)		
High	156	0 (0.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
471	0.41 (0.14,1.18)	0.051

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for occupation because of the sparse number of participants with a low free testosterone level.

Table 16-27. Analysis of Free Testosterone (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Low	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,189	20 (1.7)		
Background RH	372	5 (1.3)	0.94 (0.35,2.55)	0.906
Low RH	234	8 (3.4)	1.95 (0.84,4.52)	0.120
High RH	238	1 (0.4)	0.21 (0.03,1.57)	0.128
Low plus High RH	472	9 (1.9)	0.63 (0.20,1.99)	0.431

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,189		
Background RH	370	0.88 (0.32,2.46)	0.811
Low RH	234	1.38 (0.57,3.35)	0.470
High RH	237	0.28 (0.04,2.21)	0.227
Low plus High RH	471	0.62 (0.19,2.01)	0.424

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Low	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	281	2 (0.7)	0.94 (0.65,1.36)	0.744
Medium	281	9 (3.2)		
High	282	3 (1.1)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 16-27. Analysis of Free Testosterone (Discrete) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
n	Analysis Results for Log_2 (1987 Dioxin + 1) Adjusted Relative Risk (95% C.I.)[a]	p-Value
841	0.94 (0.52,1.70)	0.835

[a] Relative risk for a twofold increase in 1987 dioxin.

Both the unadjusted and adjusted Model 2 analyses revealed significant relations between initial dioxin and free testosterone (Table 16-27(c,d): Est. RR=0.46, p=0.019; Adj. RR=0.41, p=0.051, respectively). The percentages of low free testosterone values within the low, medium, and high initial dioxin categories were 3.2, 2.5, and 0.0, respectively.

The unadjusted and adjusted Models 3 and 4 analyses were nonsignificant (Table 16-27(e–h): p≥0.12 for each analysis).

16.2.2.3.20 Estradiol (Continuous)

Unadjusted and adjusted Model 1 analyses of estradiol in its continuous form did not reveal significant overall group differences between Ranch Hands and Comparisons (Table 16-28(a,b): p>0.38 for each analysis). After stratifying by occupation, a significant difference was seen between Ranch Hand officers and Comparison officers in both the unadjusted and adjusted analyses (Table 16-28(a,b): difference of means=–3.43 pg/ml, p=0.003, for unadjusted; difference of adjusted means=–3.55 pg/ml, p=0.003, for adjusted). The adjusted mean estradiol value for Ranch Hand officers was 40.35 pg/ml versus a mean value of 43.90 pg/ml for Comparison officers.

Table 16-28. Analysis of Estradiol (pg/ml) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***870***	***40.06***	***–0.57 --***	***0.434***
	Comparison	***1,251***	***40.63***		
Officer	Ranch Hand	341	38.38	–3.43 --	0.003
	Comparison	494	41.81		
Enlisted Flyer	Ranch Hand	151	42.87	2.17 --	0.238
	Comparison	187	40.70		
Enlisted Groundcrew	Ranch Hand	378	40.49	0.89 --	0.418
	Comparison	570	39.60		

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

Table 16-28. Analysis of Estradiol (pg/ml) (Continuous) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***870***	***42.18***	***–0.65 --***	***0.384***
	Comparison	***1,251***	***42.83***		
Officer	Ranch Hand	341	40.35	–3.55 --	0.003
	Comparison	494	43.90		
Enlisted Flyer	Ranch Hand	151	44.77	2.21 --	0.241
	Comparison	187	42.56		
Enlisted Groundcrew	Ranch Hand	378	42.26	0.89 --	0.427
	Comparison	570	41.37		

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	160	38.37	38.41	0.007	0.084 (0.049)	0.087
Medium	162	42.23	42.24			
High	160	41.37	41.32			

[a] Transformed from square root scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on square root of estradiol versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	160	40.16	0.019	0.046 (0.057)	0.423
Medium	162	42.95			
High	160	41.36			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of estradiol versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 16-28. Analysis of Estradiol (pg/ml) (Continuous) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	**n**	**Mean[a]**	**Adj. Mean[ab]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]**	**p-Value[d]**
Comparison	1,213	40.69	40.68		
Background RH	381	39.50	39.71	–0.97 --	0.323
Low RH	239	39.65	39.58	–1.10 --	0.350
High RH	243	41.64	41.43	0.75 --	0.523
Low plus High RH	482	40.65	40.51	–0.17 --	0.852

[a] Transformed from square root scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[d] P-value is based on difference of means on square root scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	**n**	**Adj. Mean[a]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]**	**p-Value[c]**
Comparison	1,213	42.96		
Background RH	381	41.76	–1.20 --	0.241
Low RH	239	41.51	–1.45 --	0.231
High RH	243	44.13	1.17 --	0.347
Low plus High RH	482	42.82	–0.14 --	0.888

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 16-28. Analysis of Estradiol (pg/ml) (Continuous) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	288	39.14	0.002	0.039 (0.031)	0.212
Medium	287	39.72			
High	288	41.57			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of estradiol versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	288	42.60	0.017	0.019 (0.036)	0.599
Medium	287	42.42			
High	288	44.00			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of estradiol versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

The unadjusted Model 2 analysis revealed a marginally significant positive association between estradiol in its continuous form and initial dioxin (Table 16-28(c): slope=0.084, p=0.087). After adjusting for covariates, the results became nonsignificant (Table 16-28(d): p=0.423).

Unadjusted and adjusted analyses for Models 3 and 4 were nonsignificant (Table 16-28(e–h): p>0.21 for each analysis).

16.2.2.3.21 Estradiol (Discrete)

The unadjusted and adjusted Model 1 analyses of estradiol in its discrete form did not reveal a significant difference between Ranch Hands and Comparisons (Table 16-29(a,b): p≥0.12 for each contrast).

Table 16-29. Analysis of Estradiol (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***870***	***236 (27.1)***	***0.96 (0.79,1.16)***	***0.666***
	Comparison	***1,251***	***350 (28.0)***		
Officer	Ranch Hand	341	80 (23.5)	0.78 (0.57,1.08)	0.131
	Comparison	494	139 (28.1)		
Enlisted Flyer	Ranch Hand	151	44 (29.1)	0.89 (0.56,1.42)	0.632
	Comparison	187	59 (31.6)		
Enlisted Groundcrew	Ranch Hand	378	112 (29.6)	1.16 (0.87,1.55)	0.319
	Comparison	570	152 (26.7)		

Table 16-29. Analysis of Estradiol (Discrete) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.95 (0.78,1.16)***	***0.619***
Officer	0.78 (0.56,1.07)	0.120
Enlisted Flyer	0.89 (0.56,1.42)	0.616
Enlisted Groundcrew	1.16 (0.87,1.55)	0.312

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	33 (20.6)	1.17 (1.00,1.36)	0.045
Medium	162	52 (32.1)		
High	160	47 (29.4)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
482	1.12 (0.94,1.33)	0.213

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,213	343 (28.3)		
Background RH	381	102 (26.8)	0.96 (0.74,1.25)	0.774
Low RH	239	59 (24.7)	0.82 (0.60,1.13)	0.234
High RH	243	73 (30.0)	1.05 (0.78,1.43)	0.731
Low plus High RH	482	132 (27.4)	0.93 (0.74,1.18)	0.566

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 16-29. Analysis of Estradiol (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Comparison	1,213		
Background RH	381	0.97 (0.75,1.27)	0.842
Low RH	239	0.79 (0.57,1.09)	0.155
High RH	243	1.05 (0.77,1.44)	0.757
Low plus High RH	482	0.91 (0.72,1.16)	0.460

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**	
1987 Dioxin	**n**	**Number (%) High**	**Estimated Relative Risk (95% C.I.)[a]**	**p-Value**
Low	288	79 (27.4)	1.04 (0.94,1.15)	0.430
Medium	287	69 (24.0)		
High	288	86 (29.9)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
863	0.99 (0.89,1.12)	0.926

[a] Relative risk for a twofold increase in 1987 dioxin.

A significant relation was seen between estradiol and initial dioxin in the unadjusted Model 2 analysis (Table 16-29(c): Est. RR=1.17, p=0.045). After adjusting for covariates, the results became nonsignificant (Table 16-29(d): p=0.213).

Unadjusted and adjusted analyses for Models 3 and 4 were nonsignificant (Table 13-29(e–h): p>0.15 for each analysis).

16.2.2.3.22 LH (Continuous)

The unadjusted and adjusted analysis of LH did not show a significant relation with dioxin in Models 1 through 3 (Table 16-30(a–f): p>0.13 for each analysis).

Table 16-30. Analysis of LH (mIU/ml) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***870***	***3.86***	***0.00 --***	***0.979***
	Comparison	***1,251***	***3.86***		
Officer	Ranch Hand	341	4.09	0.27 --	0.131
	Comparison	494	3.82		
Enlisted Flyer	Ranch Hand	151	3.67	–0.34 --	0.194
	Comparison	187	4.02		
Enlisted Groundcrew	Ranch Hand	378	3.74	–0.11 --	0.491
	Comparison	570	3.85		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***870***	***3.84***	***–0.01 --***	***0.955***
	Comparison	***1,251***	***3.85***		
Officer	Ranch Hand	341	3.85	0.22 --	0.185
	Comparison	494	3.63		
Enlisted Flyer	Ranch Hand	151	3.55	–0.37 --	0.147
	Comparison	187	3.92		
Enlisted Groundcrew	Ranch Hand	378	4.03	–0.08 --	0.650
	Comparison	570	4.10		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	160	3.84	3.84	0.001	–0.016 (0.023)	0.496
Medium	162	3.82	3.82			
High	160	3.66	3.65			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of LH versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 16-30. Analysis of LH (mIU/ml) (Continuous) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)**		
Initial Dioxin	**n**	**Adj. Mean[a]**	**R^2**	**Adj. Slope (Std. Error)[b]**	**p-Value**
Low	160	3.65	0.014	–0.008 (0.027)	0.755
Medium	162	3.67			
High	160	3.56			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of LH versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	**n**	**Mean[a]**	**Adj. Mean[ab]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]**	**p-Value[d]**
Comparison	1,213	3.85	3.85		
Background RH	381	4.04	4.01	0.16 --	0.264
Low RH	239	3.82	3.83	–0.02 --	0.900
High RH	243	3.72	3.74	–0.11 --	0.504
Low plus High RH	482	3.77	3.78	–0.07 --	0.601

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 16-30. Analysis of LH (mIU/ml) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	**n**	**Adj. Mean[a]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]**	**p-Value[c]**
Comparison	1,213	3.84		
Background RH	381	4.00	0.16 --	0.281
Low RH	239	3.73	–0.11 --	0.479
High RH	243	3.81	–0.03 --	0.839
Low plus High RH	482	3.77	–0.07 --	0.553

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin +1)**		
1987 Dioxin	**n**	**Mean[a]**	**R^2**	**Adjusted Slope (Std. Error)[b]**	**p-Value**
Low	288	4.15	0.005	–0.030 (0.015)	0.042
Medium	287	3.75			
High	288	3.77			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of LH versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**		
1987 Dioxin	**n**	**Adj. Mean[a]**	**R^2**	**Adjusted Slope (Std. Error)[b]**	**p-Value**
Low	288	4.13	0.034	–0.024 (0.017)	0.149
Medium	287	3.67			
High	288	3.87			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of LH versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

The unadjusted Model 4 analysis revealed a significant inverse association between LH in its continuous form and 1987 dioxin (Table 16-30(g): slope=–0.030, p=0.042). After adjusting for covariates, the results became nonsignificant (Table 16-30(h): p=0.149).

16.2.2.3.23 LH (Discrete)

All unadjusted and adjusted analyses in Models 1, 2, and 3 showed no significant relation between group or dioxin and the discrete form of LH (Table 16-31(a–f): p≥0.28 for each analysis). A marginally significant inverse association was seen between 1987 dioxin and LH in the unadjusted Model 4 analysis (Table 16-31(g): Est. RR=0.84, p=0.094). After adjusting for covariates, the results became nonsignificant (Table 16-31(h): p=0.154).

Table 16-31. Analysis of LH (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***870***	***49 (5.6)***	***1.01 (0.69,1.47)***	***0.971***
	Comparison	***1,251***	***70 (5.6)***		
Officer	Ranch Hand	341	24 (7.0)	1.26 (0.72,2.21)	0.422
	Comparison	494	28 (5.7)		
Enlisted Flyer	Ranch Hand	151	6 (4.0)	0.93 (0.31,2.73)	0.889
	Comparison	187	8 (4.3)		
Enlisted Groundcrew	Ranch Hand	378	19 (5.0)	0.83 (0.47,1.49)	0.538
	Comparison	570	34 (6.0)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.02 (0.70,1.50)***	***0.907***
Officer	1.24 (0.70,2.20)	0.458
Enlisted Flyer	0.86 (0.29,2.55)	0.782
Enlisted Groundcrew	0.88 (0.49,1.59)	0.674

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	8 (5.0)	0.93 (0.65,1.32)	0.668
Medium	162	7 (4.3)		
High	160	6 (3.8)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 16-31. Analysis of LH (Discrete) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
482	0.97 (0.65,1.43)	0.873

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,213	67 (5.5)		
Background RH	381	27 (7.1)	1.27 (0.79,2.02)	0.322
Low RH	239	12 (5.0)	0.91 (0.48,1.71)	0.770
High RH	243	9 (3.7)	0.68 (0.33,1.38)	0.280
Low plus High RH	482	21 (4.4)	0.78 (0.47,1.30)	0.345

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,213		
Background RH	381	1.28 (0.79,2.08)	0.313
Low RH	239	0.83 (0.44,1.58)	0.573
High RH	243	0.76 (0.36,1.60)	0.475
Low plus High RH	482	0.80 (0.47,1.34)	0.392

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 16-31. Analysis of LH (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	21 (7.3)	0.84 (0.68,1.04)	0.094
Medium	287	15 (5.2)		
High	288	12 (4.2)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
863	0.84 (0.66,1.07)	0.154

[a] Relative risk for a twofold increase in 1987 dioxin.

16.2.2.3.24 FSH (Continuous)

The Model 1 unadjusted analysis of FSH did not show an overall group difference between Ranch Hands and Comparisons (Table 16-32(a): p=0.666). Stratifying by occupation revealed a marginally significant difference between Ranch Hands and Comparisons within the officer stratum (Table 16-32(a): difference of means=0.51 mIU/ml, p=0.071). The mean FSH value for Ranch Hand officers was 6.62 mIU/ml versus 6.11 mIU/ml for Comparison officers. The adjusted analysis of FSH revealed no significant difference between Ranch Hands and Comparisons across all occupations or within each occupational stratum (Table 16-32(b): p>0.11 for each contrast).

Table 16-32. Analysis of FSH (mIU/ml) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***870***	***6.05***	***0.07 --***	***0.666***
	Comparison	***1,251***	***5.98***		
Officer	Ranch Hand	341	6.62	0.51 --	0.071
	Comparison	494	6.11		
Enlisted Flyer	Ranch Hand	151	6.02	0.03 --	0.941
	Comparison	187	5.99		
Enlisted Groundcrew	Ranch Hand	378	5.59	–0.27 --	0.257
	Comparison	570	5.86		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 16-32. Analysis of FSH (mIU/ml) (Continuous) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***870***	***5.92***	***0.06 --***	***0.689***
	Comparison	***1,251***	***5.85***		
Officer	Ranch Hand	341	6.01	0.40 --	0.112
	Comparison	494	5.62		
Enlisted Flyer	Ranch Hand	151	5.67	–0.03 --	0.928
	Comparison	187	5.70		
Enlisted Groundcrew	Ranch Hand	378	6.06	–0.21 --	0.401
	Comparison	570	6.27		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	160	6.40	6.42	0.008	–0.035 (0.021)	0.099
Medium	162	5.87	5.87			
High	160	5.64	5.62			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of FSH versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	160	5.82	0.051	–0.007 (0.024)	0.763
Medium	162	5.50			
High	160	5.53			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of FSH versus $\log_2$ (initial dioxin).

Note: Low = 27-63 ppt; Medium = >63-152 ppt; High = >152 ppt.

Table 16-32. Analysis of FSH (mIU/ml) (Continuous) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,213	5.97	5.97		
Background RH	381	6.21	6.21	0.24 --	0.283
Low RH	239	6.28	6.28	0.31 --	0.258
High RH	243	5.66	5.66	–0.31 --	0.229
Low plus High RH	482	5.96	5.96	–0.01 --	0.955

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,213	5.87		
Background RH	381	6.02	0.15 --	0.491
Low RH	239	5.98	0.11 --	0.668
High RH	243	5.83	–0.04 --	0.855
Low plus High RH	482	5.90	0.03 --	0.877

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 16-32. Analysis of FSH (mIU/ml) (Continuous) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	288	6.34	0.003	–0.024 (0.015)	0.105
Medium	287	6.19			
High	288	5.70			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of FSH versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	288	6.18	0.066	–0.001 (0.016)	0.958
Medium	287	5.93			
High	288	5.97			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of FSH versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

A marginally significant inverse association was revealed between initial dioxin and FSH in the unadjusted Model 2 analysis (Table 16-32(c): slope=–0.035, p=0.099). After adjusting for covariates, the results became nonsignificant (Table 16-32(d): p=0.763).

No significant associations were revealed between FSH and dioxin in the unadjusted and adjusted Models 3 and 4 analyses (Table 16-32(e–h): p>0.10 for each analysis).

16.2.2.3.25 FSH (Discrete)

All unadjusted and adjusted analyses in Models 1 through 4 showed no significant relations between dioxin and dichotomized FSH (Table 16-33(a–h): p>0.17 for each analysis).

Table 16-33. Analysis of FSH (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***870***	***72 (8.3)***	***1.06 (0.77,1.46)***	***0.713***
	Comparison	***1,251***	***98 (7.8)***		
Officer	Ranch Hand	341	39 (11.4)	1.20 (0.77,1.88)	0.424
	Comparison	494	48 (9.7)		
Enlisted Flyer	Ranch Hand	151	17 (11.3)	1.57 (0.75,3.29)	0.235
	Comparison	187	14 (7.5)		
Enlisted Groundcrew	Ranch Hand	378	16 (4.2)	0.66 (0.36,1.20)	0.171
	Comparison	570	36 (6.3)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.04 (0.75,1.45)***	***0.794***
Officer	1.18 (0.74,1.85)	0.488
Enlisted Flyer	1.49 (0.70,3.17)	0.297
Enlisted Groundcrew	0.68 (0.37,1.26)	0.221

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	13 (8.1)	0.94 (0.72,1.22)	0.618
Medium	162	14 (8.6)		
High	160	9 (5.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
482	1.11 (0.81,1.53)	0.508

[a] Relative risk for a twofold increase in initial dioxin.

Table 16-33. Analysis of FSH (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,213	93 (7.7)		
Background RH	381	35 (9.2)	1.22 (0.81,1.84)	0.341
Low RH	239	20 (8.4)	1.10 (0.66,1.82)	0.713
High RH	243	16 (6.6)	0.85 (0.49,1.47)	0.557
Low plus High RH	482	36 (7.5)	0.96 (0.64,1.44)	0.860

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,213		
Background RH	381	1.10 (0.72,1.69)	0.652
Low RH	239	0.93 (0.55,1.56)	0.781
High RH	243	1.16 (0.64,2.08)	0.621
Low plus High RH	482	1.04 (0.68,1.58)	0.859

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	24 (8.3)	0.97 (0.82,1.15)	0.712
Medium	287	28 (9.8)		
High	288	19 (6.6)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 16-33. Analysis of FSH (Discrete) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
863	1.16 (0.93,1.45)	0.188

[a] Relative risk for a twofold increase in 1987 dioxin.

16.2.3 Longitudinal Analysis

Longitudinal analyses were conducted on the composite diabetes indicator, TSH, fasting glucose, 2-hour postprandial glucose, and total testosterone to examine whether changes across time differed with respect to group membership (Model 1), initial dioxin (Model 2), and categorized dioxin (Model 3). Model 4 was not examined in the longitudinal analysis because 1987 dioxin—the measure of exposure in these models—changes over time and is not available for all participants for 1982 or 1997.

Discrete and continuous analyses were performed for TSH, fasting glucose, 2-hour postprandial glucose, and total testosterone. The longitudinal analyses for all of these variables investigated the difference between the 1982 and 1997 examinations. These analyses were used to investigate the temporal effects of dioxin during the 15-year period between 1982 and 1997.

Participants who were abnormal in 1982 were not included in the longitudinal analysis of discrete dependent variables. The purpose of the longitudinal analysis was to examine the effects of dioxin exposure across time. Participants who were abnormal in 1982 were not considered to be at risk for developing the condition because the condition already existed at the time of the first collection of data for the AFHS (1982). Only participants who were normal at the 1982 examination were considered to be at risk for developing the disease; therefore, the rate of abnormalities under this restriction approximates an incidence rate between 1982 and 1997. That is, an incidence rate is a measure of the rate at which people without a condition develop the condition during a specified period of time (50). Summary statistics are provided for reference purposes for the 1985, 1987, and 1992 examinations.

The longitudinal analysis for the discrete form of the dependent variables examined relative risks at the 1997 examination for participants who were classified as normal at the 1982 examination. The adjusted relative risks estimated from each of the three models were used to investigate the change in the dependent variable over time. All three models were adjusted for age; Models 2 and 3 also were adjusted for the percentage of body fat at the time of the blood measurement of dioxin.

The longitudinal analysis of continuous variables examined the paired difference between the measurements from 1982 and 1997. These paired differences measured the change in the dependent variable over time. Each of the three models used in the longitudinal analysis was adjusted for age and the dependent variable as measured in 1982 (see Chapter 7, Statistical Methods).

The cutpoints for TSH, fasting glucose, 2-hour postprandial glucose, and total testosterone differed between examinations. The cutpoints changed between examinations because a different laboratory was used to perform the analysis or because an upgrade in the equipment used caused a change in the reference values. These cutpoints were used for determining abnormal and normal classifications for each of the respective examinations and are shown in Table 16-34.

Table 16-34. Normal Ranges from Air Force Health Study Examinations for Dependent Variables Used in Endocrine Longitudinal Analysis

Dependent Variable (Units)	Examination 1982	1985	1987	1992	1997
TSH (μIU/ml)	≤10	≤3	≤3	≤5.5	≤5.5
Fasting Glucose (mg/dl)	≤115 (Age < 50) ≤125 (Age ≥ 50)	≤110	≤110	≤115	≤110
2-hour Postprandial Glucose (mg/dl)	≤120	≤140	≤140	≤140	≤140
Total Testosterone (ng/dl)	≥400	≥260	≥260	≥260	≥241 (Age < 50) ≥230 (Age ≥ 50)

16.2.3.1 Medical Records Variables

16.2.3.1.1 Composite Diabetes Indicator

A participant was considered diabetic in the composite diabetes indicator variable if he had a verified history of diabetes or a 2-hour postprandial glucose level of at least 200 mg/dl.

The Model 1 analysis of diabetic participants in 1997 who were nondiabetic in 1982 did not uncover a significant difference between Ranch Hands and Comparisons across all occupations or within each occupational stratum (Table 16-35(a): p≥0.66 for each analysis).

Table 16-35. Longitudinal Analysis of Composite Diabetes Indicator

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) Diabetic /(n) Examination 1982	1985	1987	1992	1997
All	***Ranch Hand***	***30 (3.7) (808)***	***52 (6.6) (791)***	***63 (8.1) (782)***	***100 (12.8) (779)***	***143 (17.7) (808)***
	Comparison	***25 (2.6) (959)***	***50 (5.3) (940)***	***64 (6.9) (931)***	***108 (11.7) (926)***	***162 (16.9) (959)***
Officer	Ranch Hand	13 (4.2) (308)	20 (6.6) (304)	23 (7.7) (300)	38 (12.6) (301)	51 (16.6) (308)
	Comparison	10 (2.6) (378)	20 (5.4) (371)	24 (6.6) (365)	43 (11.5) (373)	60 (15.9) (378)
Enlisted Flyer	Ranch Hand	5 (3.4) (145)	11 (7.7) (143)	12 (8.5) (141)	20 (14.2) (141)	26 (17.9) (145)
	Comparison	5 (3.5) (142)	7 (5.0) (141)	9 (6.4) (140)	18 (13.0) (138)	27 (19.0) (142)
Enlisted Groundcrew	Ranch Hand	12 (3.4) (355)	21 (6.1) (344)	28 (8.2) (341)	42 (12.5) (337)	66 (18.6) (355)
	Comparison	10 (2.3) (439)	23 (5.4) (428)	31 (7.3) (426)	47 (11.3) (415)	75 (17.1) (439)

Table 16-35. Longitudinal Analysis of Composite Diabetes Indicator (Continued)

Occupational Category	Group	Normal in 1982: n in 1997	Normal in 1982: Number (%) Diabetic in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***778***	***113 (14.5)***	***1.00 (0.76,1.31)***	***0.993***
	Comparison	***934***	***137 (14.7)***		
Officer	Ranch Hand	295	38 (12.9)	0.94 (0.60,1.49)	0.801
	Comparison	368	50 (13.6)		
Enlisted Flyer	Ranch Hand	140	21 (15.0)	0.93 (0.48,1.79)	0.821
	Comparison	137	22 (16.1)		
Enlisted Groundcrew	Ranch Hand	343	54 (15.7)	1.09 (0.73,1.63)	0.660
	Comparison	429	65 (15.2)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who were not diabetic in 1982 (see Chapter 7, Statistical Methods).

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN

Initial Dioxin	Number (%) Diabetic /(n) Examination: 1982	1985	1987	1992	1997
Low	6 (4.0) (151)	10 (6.7) (149)	11 (7.3) (151)	23 (16.0) (144)	32 (21.2) (151)
Medium	7 (4.5) (155)	13 (8.6) (152)	12 (7.9) (151)	25 (16.4) (152)	35 (22.6) (155)
High	8 (5.2) (153)	16 (10.7) (150)	21 (14.1) (149)	25 (16.9) (148)	39 (25.5) (153)

Initial Dioxin	Initial Dioxin Category Summary Statistics, Normal in 1982: n in 1997	Number (%) Diabetic in 1997	Analysis Results for Log_2 (Initial Dioxin)[a]: Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	145	26 (17.9)	1.28 (1.04,1.57)	0.019
Medium	148	28 (18.9)		
High	145	31 (21.4)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who were not diabetic in 1982 (see Chapter 7, Statistical Methods).

Table 16-35. Longitudinal Analysis of Composite Diabetes Indicator (Continued)

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY					
	Number (%) Diabetic/(n) Examination				
Dioxin Category	1982	1985	1987	1992	1997
Comparison	24 (2.6) (932)	47 (5.1) (916)	61 (6.7) (906)	103 (11.4) (900)	154 (16.5) (932)
Background RH	9 (2.6) (345)	13 (13.9) (337)	19 (5.8) (328)	27 (8.1) (332)	35 (10.1) (345)
Low RH	11 (4.9) (226)	18 (8.1) (221)	18 (8.1) (223)	36 (16.6) (217)	49 (21.7) (226)
High RH	10 (4.3) (233)	21 (9.1) (230)	26 (11.4) (228)	37 (16.3) (227)	57 (24.5) (233)
Low plus High RH	21 (4.6) (459)	39 (8.6) (451)	44 (9.8) (451)	73 (16.4) (444)	106 (23.1) (459)

	Normal in 1982			
Dioxin Category	n in 1997	Number (%) Diabetic in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	908	130 (14.3)		
Background RH	336	26 (7.7)	0.55 (0.35,0.88)	0.012
Low RH	215	38 (17.7)	1.11 (0.72,1.71)	0.634
High RH	223	47 (21.1)	1.61 (1.07,2.42)	0.023
Low plus High RH	438	85 (19.4)	1.34 (0.97,1.86)	0.079

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who were not diabetic in 1982 (see Chapter 7, Statistical Methods).

The Model 2 longitudinal analysis revealed a significant positive association between initial dioxin and the percentage of diabetic participants (Table 16-35(b): Adj. RR=1.28, p=0.019). The percentages of diabetic participants in 1997 who were nondiabetic in 1982 were 17.9, 18.9, and 21.4 in the low, medium, and high initial dioxin categories, respectively.

Three significant contrasts were seen in the Model 3 longitudinal analysis of composite diabetes indicator: Ranch Hands in the background dioxin category versus Comparisons (Table 16-35(c): Adj. RR=0.55, p=0.012), Ranch Hands in the high dioxin category versus Comparisons (Table 16-35(c): Adj. RR=1.61, p=0.023), and Ranch Hands in the low plus high dioxin category versus Comparisons (Table 16-35(c): Adj. RR=1.34, p=0.079). The percentages of participants who were nondiabetic in 1982 and diabetic in 1997 were 7.7, 21.1, 19.4, and 14.3 for Ranch Hands in the background dioxin category, Ranch Hands in

the high dioxin category, Ranch Hands in the low plus high dioxin category, and Comparisons, respectively.

16.2.3.2 Laboratory Examination Variables

16.2.3.2.1 TSH (Continuous)

The longitudinal analyses in Models 1 through 3 did not reveal a significant association between dioxin and change in mean TSH level (Table 16-36(a–c): p>0.26 for each analysis).

Table 16-36. Longitudinal Analysis of TSH (μIU/ml) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS									
		Mean[a]/(n) Examination							
Occupational Category	Group	1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	***Ranch Hand***	***3.64 (791)***	***1.21 (773)***	***0.91 (762)***	***1.60 (770)***	***1.87 (791)***	***−1.76***	***−0.06***	***0.525***
	Comparison	***3.49 (929)***	***1.16 (911)***	***0.87 (904)***	***1.56 (910)***	***1.79 (929)***	***−1.70***		
Officer	Ranch Hand	3.78 (298)	1.28 (294)	0.99 (289)	1.73 (293)	2.00 (298)	−1.78	−0.15	0.700
	Comparison	3.47 (358)	1.18 (352)	0.89 (347)	1.62 (353)	1.84 (358)	−1.63		
Enlisted Flyer	Ranch Hand	3.46 (141)	1.16 (138)	0.84 (135)	1.43 (139)	1.72 (141)	−1.74	0.03	0.440
	Comparison	3.66 (139)	1.15 (138)	0.87 (137)	1.53 (137)	1.89 (139)	−1.77		
Enlisted Groundcrew	Ranch Hand	3.59 (352)	1.17 (341)	0.89 (338)	1.56 (338)	1.83 (352)	−1.76	−0.02	0.263
	Comparison	3.45 (432)	1.15 (421)	0.84 (420)	1.52 (420)	1.71 (432)	−1.74		

[a] Transformed from natural logarithm scale.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of natural logarithm of TSH; results adjusted for natural logarithm of TSH in 1982 and age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

Table 16-36. Longitudinal Analysis of TSH (μIu/ml) (Continuous)

(b) MODEL 2: RANCH HANDS – INITIAL DIOXIN							
Initial Dioxin Category Summary Statistics						Analysis Results for Log_2 (Initial Dioxin)[b]	
	Mean[a]/(n) Examination						
Initial Dioxin	1982	1985	1987	1992	1997	Adjusted Slope (Std. Error)	p-Value
Low	3.62 (151)	1.22 (148)	0.95 (150)	1.60 (146)	1.94 (151)	–0.007 (0.020)	0.717
Medium	3.56 (155)	1.23 (152)	0.91 (151)	1.57 (153)	1.86 (155)		
High	3.59 (145)	1.17 (142)	0.89 (140)	1.55 (142)	1.80 (145)		

[a] Transformed from natural logarithm scale.

[b] Results based on difference between natural logarithm of 1997 TSH and natural logarithm of 1982 TSH versus $\log_2$ (initial dioxin); results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of 1982 TSH, and age in 1997.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY								
	Mean[a]/(n) Examination							
Dioxin Category	1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
Comparison	3.49 (901)	1.16 (886)	0.86 (878)	1.56 (883)	1.79 (901)	–1.70		
Background RH	3.69 (334)	1.21 (326)	0.91 (316)	1.63 (324)	1.87 (334)	–1.81	–0.11	0.934
Low RH	3.58 (224)	1.23 (218)	0.95 (221)	1.61 (217)	1.90 (224)	–1.67	0.03	0.514
High RH	3.60 (227)	1.18 (224)	0.88 (220)	1.54 (224)	1.83 (227)	–1.77	–0.07	0.681
Low plus High RH	3.59 (451)	1.21 (442)	0.91 (441)	1.57 (441)	1.87 (451)	–1.72	–0.02	0.492

[a] Transformed from natural logarithm scale.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of natural logarithm of 1997 TSH; results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of 1982 TSH, and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

16.2.3.2.2 TSH (Discrete)

The longitudinal analysis of high 1997 TSH levels for participants who had normal TSH levels in 1982 was not significantly associated with group or dioxin in Models 1 through 3 (Table 16-37(a–c): p>0.23 for each analysis).

Table 16-37. Longitudinal Analysis of TSH (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) High/(n) Examination 1982	1985	1987	1992	1997
All	***Ranch Hand***	***5 (0.6) (791)***	***9 (1.2) (773)***	***10 (1.3) (762)***	***10 (1.3) (770)***	***32 (4.0) (791)***
	Comparison	***4 (0.4) (929)***	***14 (1.5) (911)***	***11 (1.2) (904)***	***19 (2.1) (910)***	***29 (3.1) (929)***
Officer	Ranch Hand	2 (0.7) (298)	4 (1.4) (294)	5 (1.7) (289)	4 (1.4) (293)	12 (4.0) (298)
	Comparison	1 (0.3) (359)	6 (1.7) (352)	5 (1.4) (347)	12 (3.4) (353)	11 (3.1) (358)
Enlisted Flyer	Ranch Hand	0 (0.0) (141)	1 (0.7) (138)	1 (0.7) (135)	2 (1.4) (139)	3 (2.1) (141)
	Comparison	1 (0.7) (139)	2 (1.4) (138)	1 (0.7) (137)	1 (0.7) (137)	5 (3.6) (139)
Enlisted Groundcrew	Ranch Hand	3 (0.9) (352)	4 (1.2) (341)	4 (1.2) (338)	4 (1.2) (338)	17 (4.8) (352)
	Comparison	2 (0.5) (432)	6 (1.4) (421)	5 (1.2) (420)	6 (1.4) (420)	13 (3.0) (432)

Occupational Category	Group	Normal in 1982 n in 1997	Number (%) High in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***786***	***28 (3.6)***	***1.23 (0.72,2.10)***	***0.454***
	Comparison	***925***	***27 (2.9)***		
Officer	Ranch Hand	296	11 (3.7)	1.20 (0.51,2.81)	0.675
	Comparison	357	11 (3.1)		
Enlisted Flyer	Ranch Hand	141	3 (2.1)	0.57 (0.13,2.45)	0.452
	Comparison	138	5 (3.6)		
Enlisted Groundcrew	Ranch Hand	349	14 (4.0)	1.63 (0.73,3.65)	0.233
	Comparison	430	11 (2.6)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal TSH level in 1982 (see Chapter 7, Statistical Methods).

Table 16-37. Longitudinal Analysis of TSH (Discrete) (Continued)

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN					
	Number (%) High/(n) Examination				
Initial Dioxin	1982	1985	1987	1992	1997
Low	0 (0.0) (151)	1 (0.7) (148)	1 (0.7) (150)	0 (0.0) (146)	6 (4.0) (151)
Medium	1 (0.6) (155)	3 (2.0) (152)	2 (1.3) (151)	1 (0.7) (153)	4 (2.6) (155)
High	1 (0.7) (145)	1 (0.7) (142)	2 (1.4) (140)	5 (3.5) (142)	7 (4.8) (145)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1982			
Initial Dioxin	n in 1997	Number (%) High in 1997	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	151	6 (4.0)	1.16 (0.78,1.72)	0.486
Medium	154	3 (1.9)		
High	144	6 (4.2)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal TSH level in 1982 (see Chapter 7, Statistical Methods).

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY					
	Number (%) High/(n) Examination				
Dioxin Category	1982	1985	1987	1992	1997
Comparison	4 (0.4) (901)	14 (1.6) (886)	11 (1.3) (878)	19 (2.2) (883)	29 (3.2) (901)
Background RH	3 (0.9) (334)	4 (1.2) (326)	5 (1.6) (316)	4 (1.2) (324)	14 (4.2) (334)
Low RH	0 (0.0) (224)	2 (0.9) (218)	2 (0.9) (221)	1 (0.5) (217)	7 (3.1) (224)
High RH	2 (0.9) (227)	3 (1.3) (224)	3 (1.4) (220)	5 (2.2) (224)	10 (4.4) (227)
Low plus High RH	2 (0.4) (451)	5 (1.1) (442)	5 (1.1) (441)	6 (1.4) (441)	17 (3.8) (451)

Table 16-37. Longitudinal Analysis of TSH (Discrete) (Continued)

Dioxin Category	Normal in 1982: n in 1997	Normal in 1982: Number (%) High in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	897	27 (3.0)		
Background RH	331	12 (3.6)	1.10 (0.55,2.22)	0.782
Low RH	224	7 (3.1)	1.01 (0.43,2.35)	0.984
High RH	225	8 (3.6)	1.42 (0.63,3.22)	0.399
Low plus High RH	449	15 (3.3)	1.20 (0.63,2.29)	0.585

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal TSH level in 1982 (see Chapter 7, Statistical Methods).

16.2.3.2.3 Fasting Glucose (Continuous)

Analysis of Models 1 through 3 showed no significant relations between dioxin and the change in mean fasting glucose between 1982 and 1997 (Table 16-38(a–c): p>0.14 for each analysis).

Table 16-38. Longitudinal Analysis of Fasting Glucose (mg/dl) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Mean[a]/(n) Examination 1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	***Ranch Hand***	***97.4 (817)***	***98.9 (799)***	***100.2 (790)***	***104.5 (795)***	***101.7 (817)***	***4.3***	***–0.3***	***0.817***
	Comparison	***96.8 (974)***	***98.0 (956)***	***99.8 (948)***	***104.1 (954)***	***101.5 (974)***	***4.6***		
Officer	Ranch Hand	98.1 (310)	100.1 (306)	101.4 (302)	105.1 (305)	101.6 (310)	3.5	–0.1	0.962
	Comparison	96.9 (380)	97.9 (374)	100.3 (368)	104.4 (375)	100.5 (380)	3.6		
Enlisted Flyer	Ranch Hand	98.2 (148)	98.4 (145)	100.5 (143)	104.4 (145)	102.8 (148)	4.6	–1.0	0.693
	Comparison	97.9 (145)	99.0 (144)	100.3 (143)	104.7 (143)	103.5 (145)	5.6		

Table 16-38. Longitudinal Analysis of Fasting Glucose (mg/dl) (Continuous) (Continued)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS									
		Mean[a]/(n) Examination							
Occupational Category	Group	1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
Enlisted Groundcrew	Ranch Hand	96.5 (359)	98.0 (348)	99.1 (345)	104.1 (345)	101.4 (359)	4.8	−0.4	0.871
	Comparison	96.4 (449)	97.7 (438)	99.3 (437)	103.6 (436)	101.6 (449)	5.2		

[a] Transformed from natural logarithm scale.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of natural logarithm of fasting glucose; results adjusted for natural logarithm of fasting glucose in 1982 and age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

(b) MODEL 2: RANCH HANDS – INITIAL DIOXIN							
Initial Dioxin Category Summary Statistics						Analysis Results for Log_2 (Initial Dioxin)[b]	
	Mean[a]/(n) Examination						
Initial Dioxin	1982	1985	1987	1992	1997	Adjusted Slope (Std. Error)	p-Value
Low	97.5 (153)	99.7 (150)	101.4 (152)	105.1 (148)	101.5 (153)	0.008 (0.007)	0.261
Medium	98.3 (158)	99.4 (155)	100.7 (155)	105.0 (155)	104.6 (158)		
High	99.2 (153)	101.3 (150)	103.4 (148)	109.6 (150)	105.5 (153)		

[a] Transformed from natural logarithm scale.
[b] Results based on difference between natural logarithm of 1997 fasting glucose and natural logarithm of 1982 fasting glucose versus $\log_2$ (initial dioxin); results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of 1982 fasting glucose, and age in 1997.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

Table 16-38. Longitudinal Analysis of Fasting Glucose (mg/dl) (Continuous) (Continued)

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY								
Dioxin Category	Mean[a]/(n) Examination 1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
Comparison	96.8 (946)	97.9 (931)	99.7 (922)	103.9 (927)	101.3 (946)	4.5		
Background RH	96.2 (347)	97.3 (339)	98.1 (330)	101.8 (337)	98.6 (347)	2.4	–2.1	0.484
Low RH	97.9 (229)	100.0 (223)	100.9 (226)	105.3 (222)	101.5 (229)	3.5	–1.0	0.312
High RH	98.7 (235)	100.1 (232)	102.7 (229)	107.7 (231)	106.3 (235)	7.5	3.0	0.146
Low plus High RH	98.3 (464)	100.1 (455)	101.8 (455)	106.5 (453)	103.9 (464)	5.5	1.0	0.755

[a] Transformed from natural logarithm scale.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of natural logarithm of 1997 fasting glucose; results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of 1982 fasting glucose, and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

16.2.3.2.4 Fasting Glucose (Discrete)

The Model 1 longitudinal analysis of high fasting glucose levels in 1997 did not reveal a significant difference between Ranch Hands and Comparisons across all occupations or within each occupational stratum (Table 16-39(a): p>0.25 for each analysis).

Table 16-39. Longitudinal Analysis of Fasting Glucose (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) High /(n) Examination 1982	1985	1987	1992	1997
All	***Ranch Hand***	***37 (4.5) (817)***	***76 (9.5) (799)***	***94 (11.9) (790)***	***106 (13.3) (795)***	***149 (18.2) (817)***
	Comparison	***34 (3.5) (974)***	***88 (9.2) (956)***	***122 (12.9) (948)***	***125 (13.1) (954)***	***158 (16.2) (974)***
Officer	Ranch Hand	12 (3.9) (310)	27 (8.8) (306)	40 (13.2) (302)	39 (12.8) (305)	54 (17.4) (310)
	Comparison	11 (2.9) (380)	33 (8.8) (374)	48 (13.0) (368)	50 (13.3) (375)	58 (15.3) (380)
Enlisted Flyer	Ranch Hand	11 (7.4) (148)	16 (11.0) (145)	18 (12.6) (143)	20 (13.8) (145)	28 (18.9) (148)
	Comparison	6 (4.1) (145)	14 (9.7) (144)	20 (14.0) (143)	17 (11.9) (143)	25 (17.2) (145)
Enlisted Groundcrew	Ranch Hand	14 (3.9) (359)	33 (9.5) (348)	36 (10.4) (345)	47 (13.6) (345)	67 (18.7) (359)
	Comparison	17 (3.8) (449)	41 (9.4) (438)	54 (12.4) (437)	58 (13.3) (436)	75 (16.7) (449)

Occupational Category	Group	Normal in 1982: n in 1997	Normal in 1982: Number (%) High in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***780***	***116 (14.9)***	***1.16 (0.88,1.52)***	***0.303***
	Comparison	***940***	***124 (13.2)***		
Officer	Ranch Hand	298	44 (14.8)	1.18 (0.76,1.85)	0.462
	Comparison	369	47 (12.7)		
Enlisted Flyer	Ranch Hand	137	17 (12.4)	0.89 (0.44,1.81)	0.758
	Comparison	139	19 (13.7)		
Enlisted Groundcrew	Ranch Hand	345	55 (15.9)	1.26 (0.84,1.89)	0.256
	Comparison	432	58 (13.4)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal fasting glucose level in 1982 (see Chapter 7, Statistical Methods).

Table 16-39. Longitudinal Analysis of Fasting Glucose (Discrete) (Continued)

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN

Initial Dioxin	Number (%) High /(n) Examination 1982	1985	1987	1992	1997
Low	10 (6.5) (153)	15 (10.0) (150)	21 (13.8) (152)	25 (16.9) (148)	28 (18.3) (153)
Medium	9 (5.7) (158)	21 (13.5) (155)	20 (12.9) (155)	23 (14.8) (155)	35 (22.2) (158)
High	11 (7.2) (153)	20 (13.3) (150)	25 (16.9) (148)	26 (17.3) (150)	38 (24.8) (153)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1982			
Initial Dioxin	n in 1997	Number (%) High in 1997	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	143	19 (13.3)	1.26 (1.02,1.56)	0.029
Medium	149	27 (18.1)		
High	142	28 (19.7)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal fasting glucose level in 1982 (see Chapter 7, Statistical Methods).

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY

Dioxin Category	Number (%) High/(n) Examination 1982	1985	1987	1992	1997
Comparison	32 (3.4) (946)	84 (9.0) (931)	117 (12.7) (922)	120 (12.9) (927)	152 (16.1) (946)
Background RH	7 (2.0) (347)	20 (5.9) (339)	27 (8.2) (330)	31 (9.2) (337)	46 (13.3) (347)
Low RH	14 (6.1) (229)	25 (11.2) (223)	31 (13.7) (226)	38 (17.1) (222)	43 (18.8) (229)
High RH	16 (6.8) (235)	31 (13.4) (232)	35 (15.3) (229)	36 (15.6) (231)	58 (24.7) (235)
Low plus High RH	30 (6.5) (464)	56 (12.3) (455)	66 (14.5) (455)	74 (16.3) (453)	101 (21.8) (464)

Table 16-39. Longitudinal Analysis of Fasting Glucose (Discrete) (Continued)

	Normal in 1982			
Dioxin Category	n in 1997	Number (%) High in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	914	120 (13.1)		
Background RH	340	40 (11.8)	1.04 (0.69,1.55)	0.867
Low RH	215	30 (14.0)	0.89 (0.56,1.42)	0.636
High RH	219	44 (20.1)	1.58 (1.04,2.39)	0.033
Low plus High RH	434	74 (17.1)	1.19 (0.84,1.68)	0.319

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal fasting glucose level in 1982 (see Chapter 7, Statistical Methods).

The Model 2 longitudinal analysis of fasting glucose revealed a significant positive association between initial dioxin and high fasting glucose values (Table 16-39(b): Adj. RR=1.26, p=0.029). In the low, medium, and high initial dioxin categories, 13.3 percent, 18.1 percent, and 19.7 percent of participants, respectively, who had normal fasting glucose levels in 1982 had high fasting glucose levels in 1997.

The Model 3 analysis of the change in percentage of abnormal fasting glucose values revealed a significant difference between Ranch Hands in the high dioxin category and Comparisons (Table 16-39(c): Adj. RR=1.58, p=0.033). For Ranch Hands in the high dioxin category, 20.1 percent had normal fasting glucose levels in 1982 and high fasting glucose levels in 1997. For Comparisons, 13.1 percent had normal fasting glucose levels in 1982 and high fasting glucose levels in 1997.

16.2.3.2.5 2-Hour Postprandial Glucose (Continuous)

The Model 1 analysis of the mean change in 2-hour postprandial glucose did not uncover a significant difference between all Ranch Hands and Comparisons (Table 16-40(a): p=0.982). Stratifying by occupation showed a marginally significant group difference in the officer stratum (Table 16-40(a): difference of means=3.8 mg/dl, p=0.096). The Ranch Hand officers had a mean increase of 17.0 mg/dl between 1982 and 1997 versus 13.2 mg/dl for the Comparison officers.

The mean change in 2-hour postprandial glucose between 1982 and 1997 was not significantly associated with dioxin in Models 2 and 3 (Table 16-40(b,c): p>0.67 for each analysis).

Table 16-40. Longitudinal Analysis of 2-Hour Postprandial Glucose (mg/dl) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS									
Occupational Category	Group	Mean[a]/(n) Examination 1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	***Ranch Hand***	***89.9 (665)***	***101.8 (651)***	***106.7 (641)***	***102.6 (641)***	***105.5 (665)***	***15.6***	***0.2***	***0.982***
	Comparison	***90.2 (797)***	***104.1 (781)***	***106.4 (775)***	***104.0 (773)***	***105.6 (797)***	***15.4***		
Officer	Ranch Hand	89.5 (257)	104.5 (254)	107.0 (250)	103.5 (251)	106.5 (257)	17.0	3.8	0.096
	Comparison	88.8 (318)	102.6 (311)	104.8 (305)	102.1 (315)	102.1 (318)	13.2		
Enlisted Flyer	Ranch Hand	91.7 (119)	100.6 (117)	108.4 (115)	103.8 (116)	107.5 (119)	15.8	–3.2	0.332
	Comparison	92.8 (115)	107.5 (115)	108.6 (114)	108.9 (114)	111.9 (115)	19.0		
Enlisted Groundcrew	Ranch Hand	89.5 (289)	99.8 (280)	105.8 (276)	101.3 (274)	103.8 (289)	14.3	–2.0	0.326
	Comparison	90.6 (364)	104.2 (355)	107.1 (356)	104.1 (344)	106.9 (364)	16.3		

[a] Transformed from natural logarithm scale.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of natural logarithm of 2-hour postprandial glucose; results adjusted for natural logarithm of 2-hour postprandial glucose in 1982 and age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

Table 16-40. Longitudinal Analysis of 2-Hour Postprandial Glucose (mg/dl) (Continuous) (Continued)

(b) MODEL 2: RANCH HANDS – INITIAL DIOXIN							
Initial Dioxin Category Summary Statistics						Analysis Results for Log₂ (Initial Dioxin)[b]	
	Mean[a]/(n) Examination						
Initial Dioxin	1982	1985	1987	1992	1997	Adjusted Slope (Std. Error)	p-Value
Low	90.8 (119)	105.4 (117)	112.3 (119)	102.0 (113)	107.8 (119)	–0.005 (0.012)	0.670
Medium	91.1 (120)	102.3 (117)	105.4 (116)	106.6 (117)	105.9 (120)		
High	92.0 (114)	99.6 (112)	106.5 (110)	102.5 (112)	107.3 (114)		

[a] Transformed from natural logarithm scale.
[b] Results based on difference between natural logarithm of 1997 2-hour postprandial glucose and natural logarithm of 1982 2-hour postprandial glucose versus $\log_2$ (initial dioxin); results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of 1982 2-hour postprandial glucose, and age in 1997.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

Table 16-40. Longitudinal Analysis of 2-Hour Postprandial Glucose (mg/dl) (Continuous) (Continued)

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY								
Dioxin Category	**Mean[a]/(n) Examination**					**Exam. Mean Change[b]**	**Difference of Exam. Mean Change**	**p-Value[c]**
	1982	**1985**	**1987**	**1992**	**1997**			
Comparison	90.1 (778)	103.9 (764)	106.5 (757)	103.7 (755)	105.7 (778)	15.6		
Background RH	88.4 (310)	101.1 (303)	105.4 (294)	101.5 (297)	103.9 (310)	15.5	−0.1	0.991
Low RH	91.3 (177)	103.9 (12)	109.8 (174)	103.1 (169)	107.6 (177)	16.3	0.7	0.689
High RH	91.2 (176)	101.0 (174)	106.4 (171)	104.3 (173)	106.4 (176)	15.1	−0.5	0.999
Low plus High RH	91.3 (353)	102.5 (346)	108.1 (345)	103.7 (342)	107.0 (353)	15.7	0.1	0.795

[a] Transformed from natural logarithm scale.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of natural logarithm of 1997 2-hour postprandial glucose; results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of 1982 2-hour postprandial glucose, and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

16.2.3.2.6 2-Hour Postprandial Glucose (Discrete)

The Model 1 analysis of the change in percentage of abnormal 2-hour postprandial glucose levels did not reveal a significant difference between Ranch Hands and Comparisons across all occupations (Table 16-41(a): p=0.795). Stratifying by occupation revealed a significant difference between Ranch Hands and Comparison officers (Table 16-41(a): Adj. RR=1.65, p=0.045). For officers with normal 2-hour postprandial glucose levels in 1982, 17.7 percent of the Ranch Hands and 11.4 percent of the Comparisons had impaired 2-hour postprandial glucose levels in 1997.

Table 16-41. Longitudinal Analysis of 2-Hour Postprandial Glucose (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) Impaired/(n) Examination 1982	1985	1987	1992	1997
All	***Ranch Hand***	***40 (6.0) (665)***	***53 (8.1) (651)***	***88 (13.7) (641)***	***80 (12.5) (641)***	***110 (16.5) (665)***
	Comparison	***57 (7.2) (797)***	***83 (10.6) (781)***	***84 (10.8) (775)***	***91 (11.8) (773)***	***132 (16.6) (797)***
Officer	Ranch Hand	14 (5.4) (257)	23 (9.1) (254)	31 (12.4) (250)	31 (12.4) (251)	50 (19.5) (257)
	Comparison	19 (6.0) (318)	27 (8.7) (311)	23 (7.5) (305)	33 (10.5) (315)	41 (12.9) (318)
Enlisted Flyer	Ranch Hand	9 (7.6) (119)	10 (8.5) (117)	21 (18.3) (115)	12 (10.3) (116)	22 (18.5) (119)
	Comparison	16 (13.9) (115)	17 (14.8) (115)	17 (14.9) (114)	20 (17.5) (114)	25 (21.7) (115)
Enlisted Groundcrew	Ranch Hand	17 (5.9) (289)	20 (7.1) (280)	36 (13.0) (276)	37 (13.5) (274)	38 (13.1) (289)
	Comparison	22 (6.0) (364)	39 (11.0) (355)	44 (12.4) (356)	38 (11.0) (344)	66 (18.1) (364)

Occupational Category	Group	Normal in 1982: n in 1997	Normal in 1982: Number (%) Impaired in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***625***	***92 (14.7)***	***1.04 (0.77,1.41)***	***0.795***
	Comparison	***740***	***106 (14.3)***		
Officer	Ranch Hand	243	43 (17.7)	1.65 (1.01,2.71)	0.045
	Comparison	299	34 (11.4)		
Enlisted Flyer	Ranch Hand	110	18 (16.4)	0.90 (0.44,1.87)	0.783
	Comparison	99	18 (18.2)		
Enlisted Groundcrew	Ranch Hand	272	31 (11.4)	0.73 (0.45,1.18)	0.199
	Comparison	342	54 (15.8)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal 2-hour postprandial glucose level in 1982 (see Chapter 7, Statistical Methods).

Table 16-41. Longitudinal Analysis of 2-Hour Postprandial Glucose (Discrete) (Continued)

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN

Initial Dioxin	Number (%) Impaired/(n) Examination 1982	1985	1987	1992	1997
Low	6 (5.0) (119)	11 (9.4) (117)	21 (17.6) (119)	15 (13.3) (113)	23 (19.3) (119)
Medium	10 (8.3) (120)	8 (6.8) (117)	14 (12.1) (116)	18 (15.4) (117)	22 (18.3) (120)
High	7 (6.1) (114)	10 (8.9) (112)	16 (14.5) (110)	14 (12.5) (112)	20 (17.5) (114)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1982			
Initial Dioxin	n in 1997	Number (%) Impaired in 1997	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	113	20 (17.7)	1.04 (0.81,1.34)	0.765
Medium	110	17 (15.5)		
High	107	18 (16.8)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal 2-hour postprandial glucose level in 1982 (see Chapter 7, Statistical Methods).

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY

Dioxin Category	Number (%) Impaired/(n) Examination 1982	1985	1987	1992	1997
Comparison	54 (6.9) (778)	80 (10.5) (764)	82 (10.8) (757)	87 (11.5) (755)	129 (16.6) (778)
Background RH	17 (5.5) (310)	24 (7.9) (303)	37 (12.6) (294)	33 (11.1) (297)	45 (14.5) (310)
Low RH	13 (7.3) (117)	15 (8.7) (172)	26 (14.9) (174)	22 (13.0) (169)	34 (19.2) (177)
High RH	10 (5.7) (176)	14 (8.0) (174)	25 (14.6) (171)	25 (14.5) (173)	31 (17.6) (176)
Low plus High RH	23 (6.5) (353)	29 (8.4) (346)	51 (14.8) (345)	47 (13.7) (342)	65 (18.4) (353)

Table 16-41. Longitudinal Analysis of 2-Hour Postprandial Glucose (Discrete) (Continued)

Dioxin Category	Normal in 1982: n in 1997	Normal in 1982: Number (%) Impaired in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	724	105 (14.5)		
Background RH	293	37 (12.6)	0.87 (0.58,1.32)	0.524
Low RH	164	28 (17.1)	1.14 (0.71,1.83)	0.584
High RH	166	27 (16.3)	1.24 (0.77,2.01)	0.382
Low plus High RH	330	55 (16.7)	1.19 (0.82,1.72)	0.356

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal 2-hour postprandial glucose level in 1982 (see Chapter 7, Statistical Methods).

The longitudinal analyses in Models 2 and 3 did not reveal a significant association between dioxin and the change in 2-hour postprandial glucose levels between 1982 and 1997 (Table 16-41(b,c): p>0.35 for each analysis).

16.2.3.2.7 Total Testosterone (Continuous)

The Model 1 analysis of the change in mean total testosterone did not reveal a significant difference between Ranch Hands and Comparisons across all occupations or within each occupational stratum (Table 16-42(a): p>0.35 for each analysis).

Table 16-42. Longitudinal Analysis of Total Testosterone (ng/dl) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Mean[a]/(n) Examination 1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	***Ranch Hand***	***640.8 (800)***	***600.6 (780)***	***532.1 (773)***	***509.6 (775)***	***424.1 (800)***	***-216.7***	***-13.1***	***0.380***
	Comparison	***626.7 (953)***	***581.6 (936)***	***525.9 (929)***	***498.3 (929)***	***423.1 (953)***	***-203.6***		
Officer	Ranch Hand	601.7 (302)	573.8 (295)	502.0 (294)	490.5 (295)	401.9 (302)	-199.8	-11.1	0.353
	Comparison	601.8 (371)	556.0 (367)	499.4 (361)	475.5 (365)	413.1 (371)	-188.7		
Enlisted Flyer	Ranch Hand	651.3 (143)	611.6 (140)	530.9 (138)	518.9 (140)	446.3 (143)	-205.0	-2.8	0.788
	Comparison	634.3 (140)	588.3 (139)	537.0 (138)	508.4 (138)	432.0 (140)	-202.2		
Enlisted Groundcrew	Ranch Hand	670.9 (355)	619.5 (345)	559.4 (341)	522.7 (340)	434.5 (355)	-236.3	-19.5	0.472
	Comparison	645.5 (442)	601.7 (430)	545.2 (430)	515.0 (426)	428.6 (442)	-216.8		

[a] Transformed from the square root of total testosterone.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of the square root of total testosterone; results adjusted for the square root of total testosterone in 1982 and age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

Table 16-42. Longitudinal Analysis of Total Testosterone (ng/dl) (Continuous) (Continued)

(b) MODEL 2: RANCH HANDS – INITIAL DIOXIN							
Initial Dioxin Category Summary Statistics						Analysis Results for Log_2 (Initial Dioxin)[b]	
	Mean[a]/(n) Examination						
Initial Dioxin	1982	1985	1987	1992	1997	Adjusted Slope (Std. Error)	p-Value
Low	639.7 (150)	573.0 (146)	515.1 (149)	507.1 (145)	404.3 (150)	0.280 (0.143)	0.051
Medium	621.7 (157)	559.1 (154)	518.1 (154)	472.9 (154)	394.7 (157)		
High	616.6 (149)	586.4 (147)	515.2 (144)	486.7 (146)	421.6 (149)		

[a] Transformed from square root of total testosterone.
[b] Results based on difference between the square root of 1997 total testosterone and the square root of 1982 total testosterone versus $\log_2$ (initial dioxin); results adjusted for percent body fat at the date of the blood measurement of dioxin, square root of 1982 total testosterone, and age in 1997.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

Table 16-42. Longitudinal Analysis of Total Testosterone (ng/dl) (Continuous) (Continued)

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY								
Dioxin Category	Mean[a]/(n) Examination 1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
Comparison	628.1 (925)	581.6 (911)	527.1 (903)	498.4 (902)	423.6 (925)	-204.5		
Background RH	662.6 (339)	639.4 (329)	554.6 (322)	540.7 (326)	448.7 (339)	-213.9	-9.4	0.789
Low RH	630.9 (225)	564.5 (218)	513.9 (222)	498.8 (218)	400.9 (225)	-230.0	-25.5	0.070
High RH	621.1 (231)	580.3 (229)	518.4 (225)	478.6 (227)	412.1 (231)	-209.0	-4.5	0.885
Low plus High RH	625.9 (456)	572.5 (447)	516.2 (447)	488.4 (445)	406.6 (456)	-219.3	-14.8	0.287

[a] Transformed from the square root of total testosterone.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of the square root of 1997 total testosterone; results adjusted for percent body fat at the date of the blood measurement of dioxin, the square root of 1982 total testosterone, and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

The Model 2 longitudinal analysis revealed a marginally significant positive association between initial dioxin and change in mean total testosterone levels (Table 16-42(b): adjusted slope=0.280, p=0.051).

The Model 3 analysis of change in mean total testosterone levels between 1982 and 1997 revealed a marginally significant difference between Ranch Hands in the low dioxin category and Comparisons (Table 16-42(c): difference of means=–25.5 ng/dl, p=0.070). The mean decrease between 1982 and 1997 for Ranch Hands in the low dioxin category was 230.0 ng/dl versus 204.5 ng/dl for Comparisons.

16.2.3.2.8 Total Testosterone (Discrete)

The longitudinal analysis in Models 1 through 3 of low total testosterone levels was not significantly associated with group or dioxin (Table 16-43(a–c): p>0.15 for each analysis).

Table 16-43. Longitudinal Analysis of Total Testosterone (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) Low /(n) Examination 1982	1985	1987	1992	1997
All	***Ranch Hand***	***37 (4.6) (800)***	***21 (2.7) (780)***	***14 (1.8) (773)***	***34 (4.4) (775)***	***67 (8.4) (800)***
	Comparison	***47 (4.9) (953)***	***24 (2.6) (936)***	***13 (1.4) (929)***	***50 (5.4) (929)***	***80 (8.4) (953)***
Officer	Ranch Hand	15 (5.0) (302)	10 (3.4) (295)	6 (2.0) (294)	14 (4.7) (295)	27 (8.9) (302)
	Comparison	20 (5.4) (371)	14 (3.8) (367)	7 (1.9) (361)	19 (5.2) (365)	30 (8.1) (371)
Enlisted Flyer	Ranch Hand	8 (5.6) (143)	4 (2.9) (140)	5 (3.6) (138)	5 (3.6) (140)	11 (7.7) (143)
	Comparison	8 (5.7) (140)	2 (1.4) (139)	1 (0.7) (138)	7 (5.1) (138)	10 (7.1) (140)
Enlisted Groundcrew	Ranch Hand	14 (3.9) (355)	7 (2.0) (345)	3 (0.9) (341)	15 (4.4) (340)	29 (8.2) (355)
	Comparison	19 (4.3) (442)	8 (1.9) (430)	5 (1.2) (430)	24 (5.6) (426)	40 (9.1) (442)

Occupational Category	Group	Normal in 1982: n in 1997	Number (%) Low in 1997	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***763***	***54 (7.1)***	***1.00 (0.69,1.46)***	***0.984***
	Comparison	***906***	***64 (7.1)***		
Officer	Ranch Hand	287	21 (7.3)	1.03 (0.56,1.87)	0.935
	Comparison	351	25 (7.1)		
Enlisted Flyer	Ranch Hand	135	9 (6.7)	1.28 (0.46,3.54)	0.637
	Comparison	132	7 (5.3)		
Enlisted Groundcrew	Ranch Hand	341	24 (7.0)	0.94 (0.54,1.62)	0.817
	Comparison	423	32 (7.6)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal total testosterone level in 1982 (see Chapter 7, Statistical Methods).

Table 16-43. Longitudinal Analysis of Total Testosterone (Discrete) (Continued)

(b) MODEL 2: RANCH HANDS — INITIAL DIOXIN

Initial Dioxin	Number (%) Low /(n) Examination 1982	1985	1987	1992	1997
Low	6 (4.0) (150)	2 (1.4) (146)	5 (3.4) (149)	5 (3.4) (145)	13 (8.7) (150)
Medium	8 (5.1) (157)	6 (3.9) (154)	2 (1.3) (154)	10 (6.5) (154)	18 (11.5) (157)
High	10 (6.7) (149)	3 (2.0) (147)	3 (2.1) (144)	10 (6.8) (146)	16 (10.7) (149)

Initial Dioxin Category Summary Statistics: Initial Dioxin	Normal in 1982: n in 1997	Number (%) Low In 1997	Analysis Results for Log_2 (Initial Dioxin)[a]: Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	144	10 (6.9)	1.04 (0.80,1.35)	0.760
Medium	149	16 (10.7)		
High	139	14 (10.1)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal total testosterone level in 1982 (see Chapter 7, Statistical Methods).

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY

Dioxin Category	Number (%) Low/(n) Examination 1982	1985	1987	1992	1997
Comparison	45 (4.9) (925)	24 (2.6) (911)	13 (1.4) (903)	49 (5.4) (902)	78 (8.4) (925)
Background RH	13 (3.8) (339)	10 (3.0) (329)	4 (1.2) (322)	9 (2.8) (326)	20 (5.9) (339)
Low RH	11 (4.9) (225)	5 (2.3) (218)	7 (3.2) (222)	7 (3.2) (218)	19 (8.4) (225)
High RH	13 (5.6) (231)	6 (2.6) (229)	3 (1.3) (225)	18 (7.9) (227)	28 (12.1) (231)
Low plus High RH	24 (5.3) (456)	11 (2.5) (447)	10 (2.2) (447)	25 (5.6) (445)	47 (10.3) (456)

Table 16-43. Longitudinal Analysis of Total Testosterone (Discrete) (Continued)

Dioxin Category	Normal in 1982: n in 1997	Normal in 1982: Number (%) Low in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	880	64 (7.3)		
Background RH	326	14 (4.3)	0.71 (0.39,1.31)	0.278
Low RH	214	16 (7.5)	0.93 (0.52,1.67)	0.812
High RH	218	24 (11.0)	1.46 (0.87,2.44)	0.153
Low plus High RH	432	40 (9.3)	1.17 (0.76,1.79)	0.482

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal total testosterone level in 1982 (see Chapter 7, Statistical Methods).

16.3 DISCUSSION

The historical, physical examination, and laboratory data analyzed in this chapter provide a comprehensive assessment of thyroid, gonadal, and endocrine pancreatic function in the population under study. The current laboratory database includes several indices relevant to the possibility that dioxin may influence glucose metabolism. The α-1-C hemoglobin measurement reflects the average blood sugar over a 3- to 4-month period and is a more accurate index of diabetic control than random or fasting blood sugar measurements. In general, participants with diabetes were of the adult-onset variety (Type 2), as associated with obesity and characterized by an acquired defect in insulin receptors with elevated serum insulin levels.

Serum levels of TSH, LH, and FSH are indices of pituitary and hypothalamic function, while the T_4 and testosterone levels reflect the integrity of the thyroid gland and testicles, respectively. Additional physical examination variables pertinent to endocrine function—body habitus, ocular signs, and deep tendon reflexes—were included in the general and neurological examinations and are reported in Chapters 9 and 11, respectively.

In the analysis of historical variables verified by a medical records review, the prevalence of thyroid disorders and diabetes was similar in the Ranch Hand and Comparison cohorts (7.5% versus 8.4% and 16.9% versus 17.0%, respectively). For Ranch Hands, in a pattern consistent with a dose-response, a significant positive association was noted between the current body burden of dioxin and the development of diabetes, specifically in the later stages requiring oral hypoglycemic and insulin therapy. Ranch Hands with higher levels of initial and 1987 serum dioxin were significantly more likely to develop diabetes sooner after their exposure than those with lower serum dioxin levels.

After analyzing the physical examination and all laboratory indices of thyroid function (T_4, TSH, and anti-thyroid antibodies), no significant group differences were defined. Consistent with the 1985, 1987, and 1992 examinations, Ranch Hands continued to have a slightly higher mean serum TSH than Comparisons (1.88 µIU/ml versus 1.81 µIU/ml), but the difference is not statistically significant. By discrete analysis, the prevalence of abnormal T_4 results was identical in the two cohorts (2.7%). In the assessment of glucose metabolism without regard to dioxin levels, no significant group differences were noted in any of the historical or laboratory variables examined, and the history of diabetes by the composite indicator was similar in the Ranch Hand and Comparison cohorts. With respect to the possibility that dioxin exposure might be a risk factor for the development of diabetes, 1987 serum dioxin levels were strongly associated, in a dose-response pattern, with abnormal elevations in fasting blood sugar in both discrete and continuous forms and with the occurrence of fasting glycosuria. Similar statistical significance ($p<0.001$) was found, by both continuous and discrete analyses, in the association of both initial and 1987 serum dioxin with elevations in α-1-C hemoglobin which, as noted above, is a more accurate reflection of blood sugar levels over time.

In the analyses of diabetic severity, Ranch Hands were significantly more likely than Comparisons to require insulin for control (2.8% versus 1.4%), particularly in the officer and enlisted groundcrew occupational groups (3.6% versus 1.4% and 2.4% versus 1.1%, respectively). Further, in a dose-response pattern, requiring insulin to treat diabetes was significantly more common in Ranch Hands with high 1987 levels of serum dioxin than in Comparisons.

In 1992, a significant association was noted between serum insulin and 1987 serum dioxin in nondiabetics. In the 1997 examination, after adjustment for covariates, no significant association was found between serum insulin and 1987 serum dioxin.

In the assessment of gonadal function, no significant group differences were defined on physical examination or with respect to the laboratory indices analyzed. Consistent with all previous examinations, mean serum levels of free and total testosterone were slightly higher in Ranch Hands than in Comparisons but differences were minimal. The unadjusted analysis of total serum testosterone yielded results consistent with a dioxin effect: total testosterone decreased as the 1987 dioxin level increased in Ranch Hands. After adjustment for covariates, the difference was no longer significant. Similar results were noted in the analyses of the biologically active free form of testosterone.

Dependent variable-covariate analyses confirmed associations that are well established in clinical practice. The classic risk factors of age, obesity, and family history of diabetes were strongly and positively associated with all diabetic indices. A significant negative association was noted between age and testicular size and serum testosterone. Blacks were at significantly greater risk for the development of diabetes by the composite indicator and by all laboratory indices of glucose metabolism.

The longitudinal analyses yielded results that would be anticipated in this aging population with no significant group differences defined. The increasing history of diabetes by the composite indicator was similar in Ranch Hands and Comparisons (17.7% versus 16.9%, respectively), as were abnormal elevations in both fasting and two-hour postprandial blood sugar (18.2% versus 16.2% and 16.5% versus 16.6%, respectively). Evidence for a dioxin effect was apparent in several analyses. In a dose-response pattern, an increasing history of diabetes was noted in Ranch Hands in the low, medium, and high initial dioxin categories (17.9%, 18.9%, and 21.4%, respectively; $p=0.019$), and Ranch Hands in the high serum dioxin category were at significantly greater risk for the development of diabetes relative to Comparisons ($RR=1.61$, $p=0.023$). In both cohorts, serum testosterone continues to decrease with advancing years.

In summary, after 15 years of observation, the prevalence of diabetes, thyroid disorders, and gonadal dysfunction remains similar in Ranch Hands and Comparisons, although significant adverse relations exist between glucose intolerance and dioxin among Ranch Hands. Although cause and effect have not

been established, the results cited above provide additional evidence for an association between diabetes and elevated serum dioxin levels.

16.4 SUMMARY

Dependent variables to assess thyroid, gonadal, and pancreatic function were examined in the endocrine assessment. Each health endpoint was examined for an association with exposure group (Model 1), initial dioxin (Model 2), categorized dioxin (Model 3), and 1987 dioxin levels (Model 4). Significant results based on adjusted analyses are discussed below.

16.4.1 Model 1: Group Analysis

The adjusted group analysis of diabetic severity showed that a greater percentage of Ranch Hands than Comparisons required insulin to treat diabetes when combining all occupations. Stratifying by occupation revealed a marginally significant increase in the need for insulin to treat diabetes for Ranch Hand officers and enlisted groundcrew. A marginally significant increase in the presence of 2-hour postprandial urinary glucose in Ranch Hands was observed when combining all occupations. Stratifying the adjusted analysis by occupation revealed Ranch Hand officers had a significantly higher prevalence of 2-hour postprandial urinary glucose than did Comparison officers.

Significant results for the thyroid function revealed a significantly greater percentage of abnormally high TSH values in Ranch Hand enlisted groundcrew than Comparison enlisted groundcrew. In addition, Comparison officers had a significantly lower mean estradiol level than Ranch Hand officers.

The results of all unadjusted and adjusted Model 1 analyses are summarized in Table 16-44.

Table 16-44. Summary of Group Analysis (Model 1) for Endocrine Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Medical Records				
Past Thyroid Disease (D)	ns	ns	NS	ns
Composite Diabetes Indicator (D)	ns	NS	ns	ns
Diabetic Severity (D):				
No Treatment vs. None	NS	ns	ns	NS
Diet Only vs. None	NS	NS	NS	NS
Oral Hypoglycemics vs. None	ns*	ns	ns	ns
Requiring Insulin vs. None	+0.026	NS*	ns	NS
Time to Diabetes Onset (C) [a]	NS	ns	NS	NS
Physical Examination				
Thyroid Gland (D)	ns	ns	NS	ns
Testicular Exam (D)	NS	ns	NS	NS
Laboratory				
TSH (C)	NS	NS	ns	NS
TSH (D):				
Low vs. Normal	NS	NS	NS	ns
High vs. Normal	NS	NS	ns	+0.044
Thyroxine (C) [a]	NS	ns	NS	NS
Thyroxine (D)	NS	NS	NS	ns

Table 16-44. Summary of Group Analysis (Model 1) for Endocrine Variables (Ranch Hands vs. Comparisons) (Continued)

	UNADJUSTED			
Variable	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Anti-Thyroid Antibodies (D)	NS	ns	NS	ns
Fasting Glucose (C)	ns	NS	ns	ns
Fasting Glucose (D)	NS	NS	NS	NS
2-Hour Postprandial Glucose (C)	NS	NS*	ns	ns
2-Hour Postprandial Glucose (D)	NS	NS*	ns	ns
Fasting Urinary Glucose (D)	ns	NS	NS	ns
2-Hour Postprandial Urinary Glucose (D)	NS	+0.034	ns	NS
Serum Insulin (C)	NS	NS	ns	ns
Serum Insulin (D):				
Low vs. Normal	ns	ns	NS	ns
High vs. Normal	ns	NS	ns	ns
α-1-C Hemoglobin (C)	ns	NS	ns	ns
α-1-C Hemoglobin (D)	NS	NS	ns	NS
Total Testosterone (C) [a]	NS	ns	NS	NS
Total Testosterone (D)	NS	NS	NS	NS
Free Testosterone (C) [a]	NS	ns	NS	NS
Free Testosterone (D)	NS	NS	NS*	ns
Estradiol (C)	ns	−0.003	NS	NS
Estradiol (D)	ns	ns	ns	NS
LH (C)	NS	NS	ns	ns
LH (D)	NS	NS	ns	ns
FSH (C)	NS	NS*	NS	ns
FSH (D)	NS	NS	NS	ns

Note: NS or ns: Not significant ($p>0.10$).
NS* or ns*: Marginally significant ($0.05<p\leq 0.10$).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00.
−: Difference of means negative.
[a] Negative difference considered adverse for this variable.

P-value given if $p\leq 0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes a relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

	ADJUSTED			
Variable	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Medical Records				
Past Thyroid Disease (D)	ns	ns	NS	ns
Composite Diabetes Indicator (D)	NS	NS	ns	NS
Diabetic Severity (D):				
No Treatment vs. None	NS	ns	ns	NS
Diet Only vs. None	NS	NS	NS	NS
Oral Hypoglycemics vs. None	ns	ns	ns	ns
Requiring Insulin vs. None	+0.017	NS*	NS	NS*
Time to Diabetes Onset (C) [a]	NS	ns	NS	ns

Table 16-44. Summary of Group Analysis (Model 1) for Endocrine Variables (Ranch Hands vs. Comparisons) (Continued)

Variable	ADJUSTED All	Officer	Enlisted Flyer	Enlisted Groundcrew
Physical Examination				
Thyroid Gland (D)	ns	ns	NS	ns
Testicular Exam (D)	NS	ns	NS	NS
Laboratory				
TSH (C)	NS	NS	ns	NS*
TSH (D):				
Low vs. Normal	NS	NS	NS	ns
High vs. Normal	NS	NS	ns	+0.037
Thyroxine (C) [a]	NS	ns	NS	NS
Thyroxine (D)	NS	NS	NS	ns
Anti-Thyroid Antibodies (D)	NS	ns	NS	ns
Fasting Glucose (C)	NS	NS	ns	ns
Fasting Glucose (D)	NS	NS	ns	NS
2-Hour Postprandial Glucose (C)	NS	NS*	ns	ns
2-Hour Postprandial Glucose (D)	ns	NS	ns	ns
Fasting Urinary Glucose (D)	ns	NS	NS	ns
2-Hour Postprandial Urinary Glucose (D)	NS*	+0.044	ns	NS
Serum Insulin (C)	NS	NS	ns	NS
Serum Insulin (D):				
Low vs. Normal	ns	ns	ns	ns
High vs. Normal	ns	NS	ns	ns
α-1-C Hemoglobin (C)	NS	NS	ns	NS
α-1-C Hemoglobin (D)	NS	NS	ns	NS*
Total Testosterone (C) [a]	ns	ns	NS	ns
Total Testosterone (D)	NS	NS	NS	NS
Free Testosterone (C) [a]	NS	ns	NS	NS
Free Testosterone (D)	NS	NS	NS*	ns
Estradiol (C)	ns	–0.003	NS	NS
Estradiol (D)	ns	ns	ns	NS
LH (C)	ns	NS	ns	ns
LH (D)	NS	NS	ns	ns
FSH (C)	NS	NS	ns	ns
FSH (D)	NS	NS	NS	ns

Note: NS or ns: Not significant ($p>0.10$).
NS* or ns*: Marginally significant ($0.05<p\leq0.10$).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00.
–: Difference of means negative.
[a] Negative difference considered adverse for this variable.

P-value given if $p\leq0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes a relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

16.4.2 Model 2: Initial Dioxin Analysis

A positive association between initial dioxin and diabetes was observed. The need for insulin to treat diabetes increased as initial dioxin increased. A marginally significant increase in the percentage of Ranch Hands taking oral hypoglycemics also was observed. The time to diabetes onset was significantly shorter for Ranch Hands with higher initial dioxin levels. The adjusted analysis of laboratory measures of diabetes revealed a positive association between initial dioxin and both fasting glucose and α-1-C hemoglobin, in both continuous and discrete forms.

A marginally significant decrease in low free testosterone levels was observed as initial dioxin increased. The results of all unadjusted and adjusted Model 2 analyses are summarized in Table 16-45.

Table 16-45. Summary of Initial Dioxin Analysis (Model 2) for Endocrine Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Past Thyroid Disease (D)	NS	NS
Composite Diabetes Indicator (D)	NS	+0.005
Diabetic Severity (D):		
No Treatment vs. None	NS	NS
Diet Only vs. None	NS	NS
Oral Hypoglycemics vs. None	NS	NS*
Requiring Insulin vs. None	NS	+0.001
Time to Diabetes Onset (C) [a]	ns	–0.013
Physical Examination		
Thyroid Gland (D)	ns	NS
Testicular Exam (D)	ns	NS
Laboratory		
TSH (C)	ns	ns
TSH (D):		
Low vs. Normal	NS	NS
High vs. Normal	NS	NS
Thyroxine (C) [a]	NS	ns
Thyroxine (D)	NS	NS
Anti-Thyroid Antibodies (D)	ns	NS
Fasting Glucose (C)	NS	+0.014
Fasting Glucose (D)	NS	+0.013
2-Hour Postprandial Glucose (C)	ns	NS
2-Hour Postprandial Glucose (D)	ns	ns
Fasting Urinary Glucose (D)	NS	NS
2-Hour Postprandial Urinary Glucose (D)	ns	ns
Serum Insulin (C)	NS	NS
Serum Insulin (D):		
Low vs. Normal	ns	ns
High vs. Normal	NS	NS
α-1-C Hemoglobin (C)	+0.009	+0.001
α-1-C Hemoglobin (D)	+0.013	+0.001
Total Testosterone (C) [a]	+0.047	ns
Total Testosterone (D)	NS	NS
Free Testosterone (C) [a]	+0.003	ns
Free Testosterone (D)	–0.019	ns*

Table 16-45. Summary of Initial Dioxin Analysis (Model 2) for Endocrine Variables (Ranch Hands Only) (Continued)

Variable	Unadjusted	Adjusted
Estradiol (C)	NS*	NS
Estradiol (D)	+0.045	NS
LH (C)	ns	ns
LH (D)	ns	ns
FSH (C)	ns*	ns
FSH (D)	ns	NS

Note: NS or ns: Not significant ($p>0.10$).
NS* or ns*: Marginally significant ($0.05<p\leq 0.10$).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00 for discrete analysis; slope nonnegative for continuous analysis.
–: Relative risk <1.00 for discrete analysis; slope negative for continuous analysis.
[a] Negative slope considered adverse for this variable.

P-value given if $p\leq 0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or slope nonnegative for continuous analysis. A lowercase "ns" denotes a relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

16.4.3 Model 3: Categorized Dioxin Analysis

The percentages of diabetes for Ranch Hands in the high dioxin category and in the low plus high dioxin category were significantly greater than for Comparisons. Ranch Hands in the background dioxin category had fewer participants taking oral hypoglycemics than did Comparisons. Ranch Hands in the low dioxin category used insulin for the treatment of diabetes more often than Comparisons. The percentages of Ranch Hands in the high dioxin category and Ranch Hands in the low plus high dioxin category requiring insulin also were significantly greater than Comparisons.

The time to diabetes onset was significantly longer for Ranch Hands in the background dioxin category than for Comparisons. Relative to Comparisons, a marginally significant decrease in the time to diabetes onset was seen for Ranch Hands in the high dioxin category and Ranch Hands in the low plus high dioxin category.

Analysis of laboratory measures of diabetes revealed a significantly higher mean α-1-C hemoglobin level for Ranch Hands in the high dioxin category than for Comparisons. A greater percentage of high α-1-C hemoglobin values was seen for Ranch Hands in the high dioxin category than for Comparisons.

The results of all unadjusted and adjusted Model 3 analyses are summarized in Table 16-46.

Table 16-46. Summary of Categorized Dioxin Analysis (Model 3) for Endocrine Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED: Background Ranch Hands vs. Comparisons	UNADJUSTED: Low Ranch Hands vs. Comparisons	UNADJUSTED: High Ranch Hands vs. Comparisons	UNADJUSTED: Low plus High Ranch Hands vs. Comparisons
Medical Records				
Past Thyroid Disease (D)	ns	ns	ns	ns
Composite Diabetes Indicator (D)	–0.041	NS	NS	NS*
Diabetic Severity (D):				
No Treatment vs. None	ns	NS	NS	NS
Diet Only vs. None	NS	NS	NS	NS
Oral Hypoglycemics vs. None	–0.006	ns	NS	NS
Requiring Insulin vs. None	NS	+0.042	+0.046	+0.013
Time to Diabetes Onset (C) [a]	+0.013	ns	ns	ns
Physical Examination				
Thyroid Gland (D)	ns	ns	ns	ns
Testicular Exam (D)	ns	NS*	NS	NS
Laboratory				
TSH (C)	NS	NS	NS	NS
TSH (D):				
Low vs. Normal	NS	ns	NS	ns
High vs. Normal	NS	ns	NS	NS
Thyroxine (C) [a]	ns	NS	NS*	NS*
Thyroxine (D)	NS	ns	NS	ns
Anti-Thyroid Antibodies (D)	NS	ns	ns	ns
Fasting Glucose (C)	ns	ns	NS	NS
Fasting Glucose (D)	ns	NS	NS*	NS
2-Hour Postprandial Glucose (C)	NS	NS	ns	NS
2-Hour Postprandial Glucose (D)	ns	NS	NS	NS
Fasting Urinary Glucose (D)	ns	ns	NS	NS
2-Hour Postprandial Urinary Glucose (D)	NS	+0.050	NS	NS
Serum Insulin (C)	ns	NS	NS	+0.046
Serum Insulin (D):				
Low vs. Normal	ns	ns	ns*	ns
High vs. Normal	ns	NS	ns	NS
α-1-C Hemoglobin (C)	ns	ns	+0.005	NS
α-1-C Hemoglobin (D)	ns	ns	+0.006	NS
Total Testosterone (C) [a]	NS	ns	NS	ns
Total Testosterone (D)	NS	NS	NS	NS
Free Testosterone (C) [a]	ns	–0.022	+0.006	NS
Free Testosterone (D)	ns	NS	ns	ns
Estradiol (C)	ns	ns	NS	ns
Estradiol (D)	ns	ns	NS	ns
LH (C)	NS	ns	ns	ns
LH (D)	NS	ns	ns	ns
FSH (C)	NS	NS	ns	ns
FSH (D)	NS	NS	ns	Ns

Table 16-46. Summary of Categorized Dioxin Analysis (Model 3) for Endocrine Variables (Ranch Hands vs. Comparisons) (Continued)

Note: NS or ns: Not significant (p>0.10).
NS* or ns*: Marginally significant (0.05<p≤0.10).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00 for discrete analysis; difference of means nonnegative for continuous analysis.
–: Relative risk <1.00.
[a] Negative difference considered adverse for this variable.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes a relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Variable	ADJUSTED Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Medical Records				
Past Thyroid Disease (D)	ns	ns	NS	ns
Composite Diabetes Indicator (D)	ns*	NS	+0.048	+0.049
Diabetic Severity (D):				
No Treatment vs. None	ns	ns	NS	NS
Diet Only vs. None	NS	NS	NS*	NS
Oral Hypoglycemics vs. None	–0.008	ns	NS	NS
Requiring Insulin vs. None	NS	+0.050	+0.009	+0.004
Time to Diabetes Onset (C) [a]	+0.021	ns	ns*	ns*
Physical Examination				
Thyroid Gland (D)	ns	ns	ns	ns
Testicular Exam (D)	ns	NS	NS	NS
Laboratory				
TSH (C)	NS	NS	NS	NS
TSH (D):				
Low vs. Normal	NS	ns	NS	ns
High vs. Normal	NS	ns	NS	NS
Thyroxine (C) [a]	NS	NS	NS	NS
Thyroxine (D)	NS	ns	NS	ns
Anti-Thyroid Antibodies (D)	NS	ns	NS	ns
Fasting Glucose (C)	ns	ns	NS	NS
Fasting Glucose (D)	ns	NS	NS*	NS
2-Hour Postprandial Glucose (C)	NS	NS	ns	NS
2-Hour Postprandial Glucose (D)	ns	NS	NS	NS
Fasting Urinary Glucose (D)	ns	ns	NS	NS
2-Hour Postprandial Urinary Glucose (D)	NS*	NS*	ns	NS
Serum Insulin (C)	ns	NS	NS	NS
Serum Insulin (D):				
Low vs. Normal	ns	ns	ns*	ns*
High vs. Normal	ns	NS	ns	ns
α-1-C Hemoglobin (C)	ns	ns	+0.022	NS
α-1-C Hemoglobin (D)	ns	ns	+0.008	NS
Total Testosterone (C) [a]	NS	ns	ns	ns
Total Testosterone (D)	ns	ns	NS*	NS

Table 16-46. Summary of Categorized Dioxin Analysis (Model 3) for Endocrine Variables (Ranch Hands vs. Comparisons) (Continued)

Variable	ADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Free Testosterone (C) [a]	NS	ns	NS	ns
Free Testosterone (D)	ns	NS	ns	ns
Estradiol (C)	ns	ns	NS	ns
Estradiol (D)	ns	ns	NS	ns
LH (C)	NS	ns	ns	ns
LH (D)	NS	ns	ns	ns
FSH (C)	NS	NS	ns	NS
FSH (D)	NS	ns	NS	NS

Note: NS or ns: Not significant (p>0.10).
NS* or ns*: Marginally significant (0.05<p≤0.10).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00 for discrete analysis; difference of means nonnegative for continuous analysis.
–: Relative risk <1.00.
[a] Negative difference considered adverse for this variable.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes a relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

16.4.4 Model 4: 1987 Dioxin Level Analysis

As 1987 dioxin levels increased, the prevalence of diabetes increased. In addition, the use of diet and oral hypoglycemics to treat diabetes increased as 1987 dioxin levels increased. Marginally significant increases with 1987 dioxin also were seen for Ranch Hands using no treatment and Ranch Hands who required insulin to treat diabetes. The time to diabetes onset was significantly shorter for Ranch Hands with higher 1987 dioxin levels.

Analyses of laboratory examination variables revealed significant positive associations between 1987 dioxin and both the continuous and discrete forms of fasting glucose and α-1-C hemoglobin. The presence of fasting urinary glucose also increased with 1987 dioxin. The results of all unadjusted and adjusted Model 4 analyses are summarized in Table 16-47.

Table 16-47. Summary of 1987 Dioxin Analysis (Model 4) for Endocrine Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Past Thyroid Disease (D)	NS	NS
Composite Diabetes Indicator (D)	+<0.001	+<0.001
Diabetic Severity (D):		
No Treatment vs. None	+0.010	NS*
Diet Only vs. None	NS	+0.048

Table 16-47. Summary of 1987 Dioxin Analysis (Model 4) for Endocrine Variables (Ranch Hands Only) (Continued)

Variable	Unadjusted	Adjusted
Oral Hypoglycemics vs. None	+<0.001	+<0.001
Requiring Insulin vs. None	NS	NS*
Time to Diabetes Onset (C) [a]	−<0.001	−<0.001
Physical Examination		
Thyroid Gland (D)	ns	NS
Testicular Exam (D)	NS	NS
Laboratory		
TSH (C)	ns	NS
TSH (D):		
Low vs. Normal	ns	NS
High vs. Normal	ns	ns
Thyroxine (C) [a]	+0.009	ns
Thyroxine (D)	ns	NS
Anti-Thyroid Antibodies (D)	ns	ns
Fasting Glucose (C)	+<0.001	+0.002
Fasting Glucose (D)	+<0.001	+0.003
2-Hour Postprandial Glucose (C)	NS	NS
2-Hour Postprandial Glucose (D)	NS	NS
Fasting Urinary Glucose (D)	+0.004	+0.006
2-Hour Postprandial Urinary Glucose (D)	ns	ns
Serum Insulin (C)	+<0.001	NS
Serum Insulin (D):		
Low vs. Normal	−0.050	ns
High vs. Normal	+0.008	NS
α-1-C Hemoglobin (C)	+<0.001	+<0.001
α-1-C Hemoglobin (D)	+<0.001	+<0.001
Total Testosterone (C) [a]	−0.003	ns
Total Testosterone (D)	+0.013	NS
Free Testosterone (C) [a]	ns	ns*
Free Testosterone (D)	ns	ns
Estradiol (C)	NS	NS
Estradiol (D)	NS	ns
LH (C)	−0.042	ns
LH (D)	ns*	ns
FSH (C)	ns	ns
FSH (D)	ns	NS

Note: NS or ns: Not significant ($p>0.10$).
NS* or ns*: Marginally significant ($0.05<p\leq 0.10$).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00 for discrete analysis; slope nonnegative for continuous analysis.
−: Relative risk <1.00 for discrete analysis; slope negative for continuous analysis.
[a] Negative slope considered adverse for this variable.

P-value given if $p\leq 0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or slope nonnegative for continuous analysis. A lowercase "ns" denotes a relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

16.5 CONCLUSION

The assessment of the endocrine system included an extensive evaluation of thyroid, pancreatic, and gonadal function and their relation to dioxin exposure. A significantly greater percentage of abnormally high TSH values was found in Ranch Hand enlisted groundcrew.

A positive association between diabetes and initial and 1987 dioxin was observed. Consistent with previous reports, the prevalence of diabetes for Ranch Hands with high dioxin levels was significantly greater than for Comparisons. A greater percentage of Ranch Hands than Comparisons used insulin to control their type 2 diabetes, primarily officers and enlisted groundcrew. The percentage of Ranch Hands requiring insulin to control their type 2 diabetes increased with initial dioxin. A greater percentage of Ranch Hands in the high dioxin category required insulin to control their type 2 diabetes than did Comparisons. The percentage of participants who treated their diabetes through diet only and the percentage of participants who used oral hypoglycemics increased with 1987 dioxin level.

The time to diabetes onset was significantly shorter for Ranch Hands with higher initial and 1987 dioxin levels. Both fasting glucose and α-1-C hemoglobin increased in Ranch Hands as initial dioxin and 1987 dioxin increased. Increased α-1-C hemoglobin levels also were observed for Ranch Hands with high dioxin levels. The presence of fasting urinary glucose also increased with 1987 dioxin.

In summary, current data reveal no relation between gonadal disorders and thyroid function and herbicide or dioxin exposure; however, current and past results indicate a consistent and potentially meaningful adverse relation between serum dioxin levels and diabetes. A significant dose-response relation was found, with Ranch Hands in the high dioxin category exhibiting an increase in disease prevalence (relative risk=1.47, 95% confidence interval: [1.00, 2.17]). A dioxin-related increase in disease severity, a decrease in the time from exposure to first diagnosis, and an increase in fasting glucose and α-1-C hemoglobin support this finding. Similar patterns were observed in 1992 and 1987.

REFERENCES

1. Wilson, J. D., and D. W. Foster, eds. 1992. *Williams Textbook of Endocrinology*. 8th ed. Philadelphia: W. B. Saunders Company.

2. Okey, A. B., D. S. Riddick, and P. A. Harper. 1994. The Ah-receptor: Mediator of toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and related compounds. *Toxicology Letters* 70(1): 1-22.

3. Lucier, G. W. 1991. Humans are sensitive species to some of the biochemical effects of structural analogs of dioxin. *Environmental Toxicology and Chemistry* 10:727-35.

4. Wang, X., R. Rosengren, V. Morrison, and S. Safe. 1992. Characterization of the human Ah receptor. *Chemosphere* 25(7-10):997-1000.

5. Cuthill, S., A. Wilhelmsson, G. G. Mason, M. Gillner, L. Poelinger, and J. A. Gustafsson. 1988. The dioxin receptor: A comparison with the glucocorticoid receptor. *Journal of Steroid Biochemistry and Molecular Biology* 30:277-80.

6. Potter, C. L., I. G. Sipes, and D. H. Russell. 1983. Hypothyroxinemia and hypothermia in rats in response to 2,3,7,8-tetrachlorodibenzo-p-dioxin administration. *Toxicology and Applied Pharmacology* 69:89-95.

7. Bastomsky, C. H. 1977. Enhanced thyroxine metabolism and high uptake goiters in rats after a single dose of 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Endocrinology* 101:292-6.

8. McKinney, J. D., J. Fawkes, S. Jordan, K. Chae, S. Oatley, R. E. Coleman, and W. Briner. 1985. 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) as a potent and persistent thyroxine agonist: A mechanistic model for toxicity based on molecular reactivity. *Environmental Health Perspectives* 61:41-53.

9. Rozman, K., T. Rozman, E. Scheufler, T. Pazdernik, and H. Greim. 1985. Thyroid hormones modulate the toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Journal of Toxicology and Environmental Health* 16:481-91.

10. Roth, W., R. Voorman, and S. D. Aust. 1988. Activity of thyroid hormone-inducible enzymes following treatment with 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Toxicology and Applied Pharmacology* 92(1):65-74.

11. Gorski, J. R., G. Muzi, L. W. D. Weber, D. W. Perera, R. J. Arceo, M. J. Latropoulos, and K. Rozman. 1988. Some endocrine and morphological aspects of the acute toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Toxicologic Pathology* 16:313-20.

12. Pohjanvirta, R., T. Kuliu, A. F. W. Morselt, R. Tuominen, R. Juvonen, K. Rozman, P. Mannisto, Y. Collan, E. L. Sainio, and J. Tuomisto. 1989. Target tissue morphology and serum biochemistry following 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) exposure in a TCDD-susceptible and a TCDD-resistant strain. *Fundamental and Applied Toxicology* 12:698-712.

13. Henry, E. C., and T. A. Gasiewicz. 1987. Changes in thyroid hormones and thyroxine glucoronidation in hamsters compared with rats following treatment with 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Toxicology and Applied Pharmacology* 84:439-53.

14. McKinney, J. D., and L. G. Pedersen. 1987. Do residue levels of polychlorinated biphenyls (PCBs) in human blood produce mild hypothyroidism? *Journal of Theoretical Biology* 129:231-41.

15. Capen, C. C. 1992. Pathophysiology of chemical injury of the thyroid gland. *Toxicology Letters* 64-65:381-8.

16. Zober, A., M. G. Ott, and P. Messerer. 1994. Morbidity follow-up study of BASF employees exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) after a 1953 chemical reactor incident. *Occupational and Environmental Medicine* 51:479-86.

17. Ott, M. G., A. Zober, and C. Germann. 1994. Laboratory results for selected target organs in 138 individuals occupationally exposed to TCDD. *Chemosphere* 29:2423-37.

18. Prokipcak, R. D., L. E. Faber, and A. B. Okey. 1989. Characterization of the Ah receptor for 2,3,7,8-tetrachlorodibenzo-p-dioxin: use of chemical crosslinking and a monoclonal antibody directed against a 59kDa protein associated with steroid receptors. *Archives of Biochemistry and Biophysics* 274:648-58.

19. Couture, L. A., B. D. Abbott, and L. S. Birnbaum. 1990. A critical review of the developmental toxicity and teratogenicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin: recent advances toward understanding the mechanism. *Teratology* 42(6):619-27.

20. Mattison, D. R., M. S. Nightingale, and E. K. Silberger. 1984. Reproductive toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin. In Lowrance, W. W., ed. *Public Health Risks of the Dioxins*. Kaufman Inc., Los Altos, California.

21. Dickerson, R., L. Johnson, and S. Safe. 1989. Effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin on androgen function in the male rat. *Toxicologist* 9:32.

22. Johnson, L., R. Dickerson, S. H. Safe, C. L. Nyberg, R. P. Lewis, and T. H. Welsh Jr. 1992. Reduced Leydig cell volume and function in adult rats exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin without a significant effect on spermatogenesis. *Toxicology* 76(2):103-18.

23. Mably, T., R. Moore, and R. Peterson. 1992. In utero and lactational exposure of male rats to 2,3,7,8-tetrachlorodibenzo-para-dioxin: 1. Effects on androgenic status. *Toxicology and Applied Pharmacology* 114(1):97-107.

24. Mably, T. A., D. L. Bjerke, R. W. Moore, A. Gendron-Fitzpatrick, and R. E. Peterson. 1992. In utero and lactational exposure of male rats to 2,3,7,8-tetrachlorodibenzo-p-dioxin: 3. Effects on spermatogenesis and reproductive capability. *Toxicology and Applied Pharmacology* 114:118-26.

25. Moore, R. W., C. L. Potter, H. M. Theobald, J. A. Robinson, and R. E. Peterson. 1985. Androgenic deficiency in male rats treated with 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Toxicology and Applied Pharmacology* 79:99-111.

26. Moore, R. W., and R. E. Peterson. 1988. Androgen catabolism and excretion in 2,3,7,8-tetrachlorodibenzo-p-dioxin-treated rats. *Biochemical Pharmacology* 37:560-2.

27. Moore, R. W., J. A. Parson, R. C. Bookstaff, and R. E. Peterson. 1989. Plasma concentrations of pituitary hormones in 2,3,7,8-tetrachlorodibenzo-p-dioxin-treated male rats. *Journal of Biochemical Toxicology* 4:165-72.

28. Bookstaff, R. C., R. W. Moore, and R. E. Peterson. 1990. 2,3,7,8-tetrachlorodibenzo-p-dioxin increases the potency of androgens and estrogens as feedback inhibitors of luteinizing hormone secretion in male rats. *Toxicology and Applied Pharmacology* 104:212-24.

29. Bookstaff, R. C., F. Kamel, R. W. Moore, D. L. Bjerke, and R. E. Peterson. 1990. Altered regulation of pituitary gonadotropin-releasing hormone (GnRH) receptor number and pituitary responsiveness to GnRH in 2,3,7,8-tetrachlorodibenzo-p-dioxin-treated male rats. *Toxicology and Applied Pharmacology* 105:78-92.

30. Gorski, J. R., M. Lebofsky, and K. Rozman. 1988. Corticosterone decreases toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in hypophysectomized rats. *Journal of Toxicology and Environmental Health* 25:349-60.

31. Bestervelt, L. L., C. J. Nolan, Y. Cai, P. Maimansomsuk, C. A. Mousigian, and W. N. Piper. 1991. Tetrachlorodibenzo-p-dioxin alters rat hypothalamic endorphin and mu-opioid receptors. *Neurotoxicology and Teratology* 13(1-6):495-7.

32. Russell, D. H., A. R. Buckley, G. N. Shah, I. G. Sipes, D. E. Blask, and B. Benson. 1988. Hypothalamic site of action of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Toxicology and Applied Pharmacology* 94:496-502.

33. Bestervelt, L. L., Y. Cai, D. W. Piper, C. J. Nolan, J. A. Pitt, and W. N. Piper. 1993. TCDD alters pituitary-adrenal function I: adrenal responsiveness to exogenous ACTH. *Neurotoxicology and Teratology* 15:365-70.

34. Bestervelt, L. L., D. W. Piper, J. A. Pitt, and W. N. Piper. 1994. Lipid peroxidation in the adrenal glands of male rats exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Toxicology Letters* 70(32):139-45.

35. Fingerhut, M. A., W. E. Halperin, D. A. Marlow, L. A. Piacitelli, P. A. Honchar, M. H. Sweeney, A. L. Greife, P. A. Dill, K. Steenland, and A. J. Suruda. 1991. Cancer mortality in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *New England Journal of Medicine* 324(4):212-8.

36. Sweeney, M. H., M. A. Fingerhut, J. C. Arezzo, R. W. Hornung, and L. B. Connally. 1993. Peripheral neuropathy after occupational exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *American Journal of Industrial Medicine* 23:845-58.

37. Egeland, G. M., M. H. Sweeney, M. A. Fingerhut, K. K. Wille, T. M. Schnorr, and W. E. Halperin. 1994. Total serum testosterone and gonadotropins in workers exposed to dioxin. *American Journal of Epidemiology* 139:272-81.

38. Henriksen, G. L., J. E. Michalek, J. A. Swaby, and A. J. Rahe. 1996. Serum dioxin, testosterone, and gonadotropins in veterans of Operation Ranch Hand. *Epidemiology* 7:352-7.

39. Pazderova-Vejlupkova, J., M. Nemcove, J. Pickova, L. Jirask, and E. Lukas. 1981. The development and prognosis of chronic intoxication by tetrachlorodibenzo-p-dioxin in men. *Archives of Environmental Health* 36:5-11.

40. Henriksen, G. L., N. S. Ketchum, J. E. Michalek, and J. A. Swaby. 1998. Serum dioxin and diabetes mellitus in veterans of Operation Ranch Hand. *Epidemiology* 9:252-8.

41. Roegner, R. H., W. D. Grubbs, M. B. Lustik, A. S. Brockman, S. C. Henderson, D. E. Williams, W. H. Wolfe, J. E. Michalek, and J. C. Miner. 1991. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Serum Dioxin Analysis of 1987 Examination Results. NTIS: AD A 237 516-24. USAF School of Medicine, Brooks Air Force Base, Texas.

42. Grubbs, W. D., W. H. Wolfe, J. E. Michalek, D. E. Williams, M. B. Lustik, A. S. Brockman, S. C. Henderson, F. R. Burnett, R. G. Land, D. J. Osborne, V. K. Rocconi, M. E. Schreiber, J. C. Miner, G. L. Henriksen, and J. A. Swaby. 1995. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final Report. 1992 Followup Examination Results. NTIS: AD A 304 306, 304 308-316. USAF School of Medicine, Brooks Air Force Base, Texas.

43. Michalek, J. E. 1998. Letter to the editor. *Epidemiology* 9:359-60.

44. Sweeney, M. H., G. M. Calvert, G. A. Egeland, M. A. Fingerhut, W. E. Halperin, L. A. Piacitelli. 1997. Review and update of the results of the NIOSH medical study of workers exposed to chemicals contaminated with 2,3,7,8-tetrachlorodibenzodioxin. *Teratogenesis, Carcinogenesis, and Mutagenesis* 17(4-5):241-7.

45. Von Benner, A., L. Edler, K. Mayer, and A. Zober. 1994. 'Dioxin' investigation program of the chemical industry professional association. *Arbeitsmedizin Sozialmedizin Praventivmedizin* 29:11-6.

46. Institute of Medicine. 1999. *Veterans and Agent Orange: Update 1998.* National Academy Press: Washington, D.C.

47. Jenkins, C. D., R. H. Roseman, and S. J. Zyzanski. 1974. Prediction of clinical coronary heart disease by a test for the coronary-prone behavior pattern. *New England Journal of Medicine* 290(23):1271-5.

48. Knapik, J. J., A. R. L. Burse, and J. A. Vogel. 1983. Height, weight, percent body fat, and indices of adiposity for young men and women entering the Army. *Aviation, Space, and Environmental Medicine* 54:223-31.

49. Michalek, J. E., J. L. Pirkle, S. P. Caudill, R. C. Tripathi, D. G. Patterson Jr., and L. L. Needham. 1996. Pharmacokinetics of TCDD in Veterans of Operation Ranch Hand: 10-year Followup. *Journal of Toxicology and Environmental Health* 47:209-20.

50. Mausner, J. S., and A. K. Bahn. 1974. *Epidemiology – An Introductory Text.* Philadelphia: W. B. Saunders Company.

Table of Contents

List of Tables

17 IMMUNOLOGIC ASSESSMENT

17.1 INTRODUCTION

17.1.1 Background

Of the many chemical compounds known to cause immune system dysfunction in laboratory animals, the polyhalogenated aromatic hydrocarbons have been the most extensively studied and, among these, 2,3,7,8-tetrachlorodibenzo-p-dioxin (dioxin) has proven to be the most toxic. Since the early 1970s, when dioxin was shown to cause marked involution of the thymus gland in experimental animals (1–4), the extensive body of literature pertinent to dioxin-induced immunotoxicity has been summarized in several review articles (5–10).

In laboratory animals, dioxin has proven to have a wide range of toxic effects on all components of the immune system, including direct thymotoxic effects, particularly on the epithelial cells (8, 11–14), compromised cell mediated (1, 13, 15–18) and humoral (1, 17, 19–22) immune function, impaired myelo- (23, 24) and lymphoproliferative (13, 25–27) responses, and suppressed complement activity (28–31).

The crucial role of the immune system in resistance to infection has been well established, and numerous animal studies have demonstrated that exposure to dioxin increases host susceptibility to a broad range of bacterial (19, 23, 29, 32, 33), parasitic (34), and viral (35, 36) infectious agents.

The role of the aryl hydrocarbon (Ah) receptor as a mediator in dioxin toxicity has been long recognized (37, 38) and summarized in numerous reviews (6, 39, 40). Much of the basic research in laboratory animals has focused on the role of the Ah receptor in some but not all manifestations of dioxin-induced immunotoxicity, including suppressed humoral (20, 22, 41–46) and cellular (47, 48) responses and impaired complement activity (49). Other studies have demonstrated that dioxin exposure can cause immune system responses independent of the Ah receptor (42, 43, 45, 50–52). Although the Ah receptor has been identified in several human tissues (see references 43, 51–53, and 55 in Chapter 9, General Health Assessment), the relevance of these observations to dioxin toxicity in humans remains unknown. In an attempt to provide data more relevant to humans, two laboratories have conducted experiments of the effects of dioxin on peripheral lymphocyte subpopulations in marmoset (52–56) and rhesus (57) monkeys. These studies were carried out in vitro, employing lymphocyte cell cultures, and in vivo, with single-dose injections of dioxin in various concentrations. In these experiments, the ratios of selected lymphocyte subsets varied inconsistently in response to the dose (high versus low) and duration (acute versus chronic) of exposure. In none of the in vivo studies did the animals demonstrate any overt illness.

The demonstration that human tonsils contain the Ah receptor (58) and the development of a tonsillar lymphocyte culture model have established a scientifically valid basis for comparison of the effects of dioxin on experimental animals and humans at the cellular level. In published results from two series of experiments, dioxin had identical effects on both human and murine B lymphocytes with dose-dependent suppression of cellular proliferation and a significant reduction in the secretion of immunoglobulins IgM and IgG (59, 60). Although the mechanism is not known, these experiments provide strong evidence that the human lymphocyte is sensitive to dioxin. These results are consistent with those reported from another laboratory investigating the effect of dioxin on human lymphocytes isolated from peripheral blood (61). As noted below, these experimental models have been applied recently to human populations exposed to dioxin (62, 63).

Immune system indices have been included in epidemiological studies of populations exposed to dioxin consequent to industrial accidents (64–72), by occupation (62, 63, 73–75), by environmental contamination (76–81), and during military service in Vietnam (82–86). Industrial accidents have resulted in the most severe human exposure to dioxin on record. In three reports published shortly after the 1976 chemical explosion in Seveso, Italy, no immune system abnormalities were found in exposed children (64, 65) or cleanup workers (66). In contrast, other investigators documented abnormal immune indices in children with chloracne (67, 68) that resolved over time and were not associated with any clinical immune deficiency illness (69, 70). Similarly, the immunologic testing abnormalities noted in a cohort of chemical workers exposed to dioxin in an industrial accident in England in 1968 were not associated with any clinical illness (71, 72).

Most of the recently published epidemiological studies have reported on the results of clinical examinations of workers who experienced significant occupational exposure to dioxin during employment at chemical factories in Germany (62, 63, 73–75). These studies, which incorporated immune system parameters in the examination protocols, are strengthened by the inclusion of serum dioxin data in the analyses. None of these studies showed any evidence in those exposed for clinical illness associated with immune system disorders nor, in relation to the body burden of dioxin, any statistically significant abnormalities in the laboratory indices.

Resident populations in the Times Beach, Missouri, area have been the subject of several studies yielding conflicting results, some of which can be attributed to methodological limitations. In two early reports, abnormalities were documented in several indices of immune function, including impaired delayed sensitivity by skin testing and nonsignificant variations in several peripheral lymphocyte subsets and ratios (76–78). In subsequent follow-up examinations of the same subjects, there were no significant differences between the exposed and control cohorts (79, 80).

A subsequent report of the subject Missouri population included serum dioxin levels that ranged from less than 20 parts per trillion (ppt) to 750 ppt. In this study, a correlation was noted between serum dioxin and an increasing percentage of CD8+ (suppressor T cells) and T_{11}+ subsets of T lymphocytes, as well as statistically nonsignificant increases in serum IgA and complement components C3 and C4 (81). As in the other Missouri studies, there was no evidence for clinical illness in the exposed cohort relative to controls.

Finally, in the 1987 and 1992 examinations of the Air Force Health Study (AFHS), multiple immunologic indices have been examined in relation to serum dioxin levels (85, 86). In the 1987 examination and, to a lesser degree, in the 1992 examination, serum IgA immunoglobulin levels were significantly higher in the Ranch Hand cohort than controls in a pattern consistent with a dose-response effect. Although of uncertain significance, this finding is of interest as one that has been noted in two other epidemiological studies cited above (74, 81) and, separately, a report of a laboratory animal study (87) that documented a selective increase in the IgA globulin fraction after a single injection of dioxin. There have been no other significant immune system differences between the Ranch Hands and Comparisons across the baseline, 1985, 1987, and 1992 examinations.

17.1.2 Summary of Previous Analyses of the Air Force Health Study

17.1.2.1 1982 Baseline Study Summary Results

Immunologic function and phenotypic marker studies were performed on 592 participants (297 Ranch Hands, 295 Comparisons) randomly selected by the terminal digit of their case number. Because of laboratory problems (e.g., fluctuating quality control and lack of simultaneous differential counts on the peripheral mononuclear cells), data could be analyzed on a group basis only.

Analyses of the cell surface markers (CD2+ or T_{11} [T cells], CD3+ or T_3 [T cells], CD4+ or T_4 [helper T cells], CD8+ or T_8 [suppressor T cells], CD20+ [B cells], the CD4–CD8 or T_4-T_8 ratio) and the total lymphocyte count (TLC) showed no significant group differences. Smoking was significantly associated with increases in most cell counts, but not with the CD4-CD8 ratio and CD20+ cells, whereas increasing age was significantly associated with decreasing TLC and CD8+ cells.

Functional studies of T and B cells via reaction to antigenic (tetanus toxoid) or mitogen (phytohemagglutinin [PHA], concanavalin A, and pokeweed) stimulation showed no group differences. Similarly, unadjusted and adjusted mean values of the four assays were not significantly different between groups.

In summary, neither immunologic function nor cell marker studies showed significant impairment in the Ranch Hand group, nor did they show patterns supportive of an herbicide effect. Smoking was associated with a significant increase in the marker cells CD2+ (T cells), CD3+ (T cells), CD4+ (helper T cells), and CD8+ (suppressor T cells), and in the TLC, with a concomitant increase in lymphocytic response to pokeweed mitogen (PWM).

17.1.2.2 1985 Follow-up Summary Results

The 1985 AFHS physical examination placed more emphasis on the immunologic assessment than did the 1982 baseline examination profile. Immunologic competence was measured by cell surface marker (phenotypic) studies and cell stimulation studies on 47 percent of the study population, and by a series of four skin test antigens in 76 percent of the participants to assess the delayed hypersensitivity response.

Surface marker studies were conducted for CD2+ cells (T cells), CD4+ cells (T cells), CD8+ cells (suppressor T cells), CD20+ (B cells), CD14+ cells (monocytes), and HLA-DR cells. The ratio of CD4 to CD8 cells also was included in the analysis. Because of inherent significant day-to-day and batch-to-batch variation, all results (including functional stimulation studies) were adjusted for blood-draw day. Statistical testing of the seven phenotypic cell markers did not reveal any significant group differences, either unadjusted or adjusted, for the covariates of age, race, occupation, current smoking, lifetime smoking history, current alcohol use, or lifetime alcohol use. Similarly, none of the unadjusted or adjusted analyses of the functional stimulation studies (for PHA, PWM, or mixed lymphocyte culture [MLC]) showed any statistically significant group differences. Overall, no pattern was identified to suggest an adverse health effect in any subgroup of either the Ranch Hands or Comparisons.

The effects of age, race, smoking, and alcohol use affected most variables in the phenotypic and stimulation studies. Consistently decreasing values of all cell markers and stimulated cells were associated with increasing age, whereas increased levels of smoking usually were associated with increases in the values of those variables. Blacks had consistently higher stimulated cell counts than non-Blacks, but this effect was not observed for counts of T cells, B cells, or HLA-DR cells. Enlisted personnel generally had higher cell surface marker counts than officers.

The delayed hypersensitivity response was assessed by the skin test antigens of mumps, *Candida albicans*, Trichophyton, and staph-phage lysate. The 48-hour measurements of skin induration and erythema for the four tests showed marked inter-reader variation. Consequently, all skin test data were declared invalid and were not used in the assessment of group differences. The skin test reading problems led to the use of additional clinical quality control procedures for the 1987 follow-up examination.

In conclusion, no significant group differences were found for the comprehensive cell surface marker or functional stimulation studies. The effects of age, smoking, and alcohol use were observed in these immunologic tests.

17.1.2.3 1987 Follow-up Study Summary Results

For the assessment of the 1987 immunologic examination data, results from a composite skin reaction test were evaluated. Various laboratory examination measurements from cell surface marker studies, three groups of functional stimulation tests, and quantitative immunoglobulins also were analyzed. Ranch Hands had a higher frequency of individuals with possibly abnormal reactions on skin testing than Comparisons. The unadjusted analyses of the laboratory examination data indicated no significant group difference between Ranch Hands and Comparisons. For the adjusted analyses of the natural killer assay measurements with and without Interleukin 2 (IL-2), significant interactions between group and race were present. The clinical meaning of these findings was not apparent and did not point to any known clinical endpoints.

17.1.2.4 Serum Dioxin Analysis of 1987 Follow-up Study Summary Results

In general, the composite skin test diagnosis results were not associated with serum dioxin levels. The Ranch Hand analyses using initial dioxin and the analyses using current dioxin and time since duty in Southeast Asia (SEA) generally displayed nonsignificant decreased risks. For the analyses contrasting Ranch Hands with unknown, low, and high current dioxin to Comparisons with background current dioxin levels, the risks were increased but nonsignificant.

For the most part, the cell surface marker variables and TLC did not display significant associations with serum dioxin. The longitudinal analyses of the CD4-CD8 ratio did not consistently show significant differences in the 1987 ratio relative to the 1985 measurement of the ratio.

For the analyses of PHA net responses, significant or marginally significant positive associations with initial dioxin were found. For the analyses involving current dioxin and time since duty in SEA, the maximum PHA net response also displayed some significant or marginally significant positive associations. Depressed immune function would be expected to demonstrate lower PHA net response.

For unstimulated MLC and MLC net response, the three statistical analysis approaches generally displayed nonsignificant associations with serum dioxin. For the analysis involving Ranch Hands in the high current dioxin category and Comparisons in the background current dioxin category, Ranch Hands had a significantly higher unstimulated MLC mean. The analyses of the natural killer cell variables generally were nonsignificant.

Significant positive associations generally were found between IgA and initial dioxin. The analyses for IgA, IgG, and IgM using current dioxin and time since duty in SEA were, for the most part, nonsignificant. For the three immunoglobulins, the overall contrasts of Ranch Hands in the unknown, low, and high current dioxin categories versus Comparisons in the background current dioxin category generally were significant or marginally significant. For IgA and IgG, the contrasts of Ranch Hands in the unknown current dioxin category versus Comparisons in the background current dioxin category were significant with Ranch Hands having lower immunoglobulin averages. For IgM, the contrasts of Ranch Hands in the low current dioxin category versus Comparisons in the background current dioxin category were marginally significant with Ranch Hands again having lower averages. Ranch Hands in the high dioxin category were not significantly different from Comparisons.

The indices of immune responses analyzed in the 1987 examination provided a comprehensive reflection of in vivo and in vitro immune function in the study population. No clinically meaningful indicators reflecting a relation between the current body burden of dioxin or the extrapolated initial exposure and immune function were found. Increased IgA levels may have represented a chronic inflammatory response to dioxin exposure. Elevated erythrocyte sedimentation rates (as discussed in the general health assessment) and increased white blood cell and platelet counts (as discussed in the hematologic

assessment) were other examples of indicators that may have represented a chronic inflammatory response to dioxin exposure.

17.1.2.5 1992 Follow-up Study Summary Results

In general, the composite skin test diagnosis results did not differ significantly between Ranch Hands and Comparisons and were not positively associated with initial or current dioxin levels. For the most part, the cell surface marker variables and total lymphocyte count did not display significant associations with serum dioxin. The longitudinal analyses of the CD4-CD8 ratio did not consistently show significant differences between the 1992 ratio relative to the 1985 measurement of the ratio.

Marginally significant positive associations were found between IgA and initial dioxin. A negative association would be expected in immunologic deficiency, but the increased IgA levels could represent a chronic inflammatory response to dioxin exposure and thus suggested long-term evaluation.

The prevalence of some lupus panel antibodies, such as the MSK smooth muscle antibody and the rheumatoid factor, decreased as dioxin exposure increased. This finding was inconsistent with a harmful effect from dioxin. The presence of lupus panel antibodies generally was considered abnormal. A smaller prevalence of the lupus panel antibodies was found in this study than would be expected in the general population. The presence of a smaller prevalence of abnormalities than expected also may have been regarded as an abnormal finding, suggesting a possible early immune alteration.

17.1.3 Parameters for the 1997 Immunologic Assessment

17.1.3.1 Dependent Variables

Table 17-1 presents the immunologic parameters evaluated and describes their medical importance. The absolute lymphocyte and immunoglobulin studies and lupus panel tests were examined for all participants, whereas the cell surface marker studies were carried out on a random sample of approximately 40 percent of the participants because of the complexity of the assay and the expense of the tests.

Table 17-1. Medical Significance of the Immunologic Data

Immunologic Measure	Rationale of the Measurement	Disease/Syndrome/Condition Endpoint
Cell Surface Marker Studies		
CD3+	Pan-T cell marker (similar to CD2 in previous AFHS examinations). Measures all mature T cells (includes CD4, CD8, etc.). Generally 70% or more of peripheral blood lymphocytes are CD3 positive.	Decrease in absolute number of T cells indicates immunodeficiency. May occur because of direct effects of malignancy (e.g., lymphoma), acquired immune deficiency syndrome (AIDS), or chemotherapy. Increase may occur in lymphoproliferative disorders or in some infections.
CD4+	Measures T cells that exhibit helper/inducer phenotype. CD4 cells initiate an immune response to processed antigens.	Markedly decreased in people with AIDS because of human immunodeficiency virus (HIV) infection of CD4+ cells; increased in autoimmune diseases.
CD8+	Measures T cells that exhibit suppressor and cytotoxic functions. Responsible for appropriate down regulation of an immune response after antigen has been cleared.	Variable in autoimmune diseases; increased in some viral illnesses and immunodeficiencies.
CD20+ (B1)	Measures peripheral blood B cells; no reaction with T cells, granulocytes, or monocytes.	Decreased result in humoral immune deficiency with impaired production of antibodies; increased in lymphoproliferative disorders.
	Double Labeled Cells (cells that express both markers)	
CD3+CD4+	Helper T cells and excludes monocytes but more specific than CD4.	Same as CD4.
CD16+56+ (CD3-)	Normally these markers do not occur on the same cells. Measures natural killer (NK) cells that can lyse foreign cells independent of antibody or prior contact with the target. CD16 is an IgG receptor that appears on NK cells and neutrophils; CD56 is more restricted to NK cells; joint use of CD16 and CD56 enhances enumeration of NK cells.	NK cells are thought to attack neoplasms and naturally prevent growth of cancers.
Absolute Lymphocytes		
	Measures absolute number of total lymphocytes circulating in peripheral blood. Major immune mechanism against fungi and viruses.	Decreased in immunodeficiency; increased in lymphoproliferative disorders.

Table 17-1. Medical Significance of the Immunologic Data (Continued)

Immunologic Measure	Rationale of the Measurement	Disease/Syndrome/Condition Endpoint
Immunoglobulins		
IgG IgA IgM	Each measures ability of specific B cell subgroup to secrete specific antibody class of molecules. Antibodies normally rise in response to infections or immunizations with bacteria, fungi, and viruses. Major immune mechanism against bacteria.	Increased in hyperglobulinemia or myeloma (monoclonal). Decreased in selective or total B cell immunodeficiency. Polyclonal increases in chronic inflammation and liver disease (cirrhosis).
Lupus Panel		
	The test composition of this profile was chosen to include the most frequently encountered autoantibodies. Presence of autoantibodies may indicate specific autoimmune diseases, especially if multiple autoantibodies are present. The individually named autoantibodies (excluding ANA and B cell clones) are associated with specific diseases. Any of these tests may also turn positive as a participant's immune system ages or otherwise is dysregulated.	
Antinuclear Antibody (ANA) Test	Screening assay (performed with monolayers of HEP-2) for many clinically meaningful autoantibodies that occur in systemic rheumatologic diseases.	Positive result suggests possible rheumatologic disease; likelihood increases with number of different positive autoantibodies.
ANA Thyroid Microsomal Antibody	Measures autoantibodies against thyroid microsomal antigen.	Present in autoimmune thyroiditis.
MSK Smooth Muscle Antibody	MSK indicates the tissues used in the assay (mouse stomach kidney); measures autoantibodies against actin in smooth muscle.	Present in autoimmune liver diseases, especially chronic active hepatitis.
MSK Mitochondrial Antibody	Measures autoantibodies against mitochondrial antigens.	Present in autoimmune liver diseases, especially primary biliary cirrhosis.
MSK Parietal Antibody	Measures autoantibodies against parietal cells of the stomach that make intrinsic factor for the absorption of vitamin B_{12}.	Present in pernicious anemia (failure to absorb vitamin B_{12}).
Rheumatoid Factor	Autoantibodies reactive with a person's own antibodies.	Present in rheumatoid arthritis; also in some infections, chronic pulmonary diseases, and other inflammatory or autoimmune diseases.

17.1.3.1.1 Laboratory Examination Data

The results of cell surface marker studies, absolute lymphocytes, quantitative immunoglobulins, and a lupus panel were analyzed. Participants who were taking anti-inflammatory medication (except aspirin and nonsteroidal) or immunosuppressant medication at the time of the 1997 physical examination were excluded from analysis. Participants who had recently received x-ray treatment or chemotherapy for cancer and participants who tested positive for HIV also were excluded from analysis.

17.1.3.1.1.1 Cell Surface Marker (Phenotypic) Studies

Quantification of the different cell populations was carried out with the use of reagent mouse monoclonal antibodies. Cell surface markers were analyzed in the statistical evaluation of the immunologic system. The unit of measurement was cells/mm^3. The CD3+CD4+ (helper T cells) double labeled cell surface marker was introduced to the AFHS for the 1997 follow-up examination.

17.1.3.1.1.2 Absolute Lymphocytes

Absolute lymphocytes indicate the density of lymphocytes in the blood. Lymphocytes recognize and destroy bacteria, fungi, viruses, and other foreign bodies. Statistical analyses were performed on absolute lymphocytes, measured in cells/mm^3.

Absolute lymphocytes also were analyzed in Chapter 15, Hematology Assessment (Table 15-19). The analysis of absolute lymphocytes in the Hematology Assessment chapter included nonreactive lymphocytes, whereas the analysis in this chapter included nonreactive and reactive lymphocytes. In addition, the analysis in this chapter included age, race, military occupation, current cigarette smoking, lifetime cigarette smoking history, current alcohol use, lifetime alcohol history, and a physical activity index as covariates. The analysis in the Hematology Assessment chapter did not include current alcohol use, lifetime alcohol history, or the physical activity index. The exclusions for analysis in the Hematology Assessment included participants with body temperatures greater than or equal to 100° Fahrenheit and participants testing positive for HIV. The exclusions in this chapter included participants who were taking anti-inflammatory (except aspirin and nonsteroidal) or immunosuppressant medication at the time of the 1997 physical examination. Participants who had recently received x-ray treatment or chemotherapy for cancer and participants who tested positive for HIV also were excluded from analysis in this chapter.

17.1.3.1.1.3 Immunoglobulins

Immunoglobulins measure the ability of a specific B cell subgroup to secrete a specific antibody class of molecules. The antibodies usually rise in response to infections or immunizations with bacteria, fungi, and viruses. Statistical analyses were performed on the immunoglobulins IgA, IgG, and IgM, measured in mg/dl.

17.1.3.1.1.4 Lupus Panel

This group of laboratory tests was configured to detect the most frequent autoantibodies found in both patients and asymptomatic individuals. Autoantibodies are markers for autoimmune diseases, and the lupus panel is considered a screening assay for a wide spectrum of autoimmune disorders (e.g., rheumatoid arthritis, systemic lupus erythematosus). Occasionally, autoantibodies are detected in asymptomatic persons; this is alternatively explained as evidence for incipient autoimmune disease or a finding of unknown meaning. In any instance, the finding of an autoantibody is not normal and should be

interpreted as an aberration of the immune system. The lupus panel was composed of the following individual tests on serum:

- Antinuclear antibody (ANA) performed on HEP-2 cells
- Mouse stomach kidney (MSK) section stain for the following specific autoantibodies:
  - Smooth muscle
  - Mitochondrial
  - Parietal cell
- Thyroid microsomal antibody
- Rheumatoid factor.

All of the autoantibodies derive from abnormalities of the B cell portion, the part of the immune system that produces immunoglobulins.

Statistical analyses were performed on the ANA, ANA thyroid microsomal antibody, MSK smooth muscle antibody, MSK mitochondrial antibody, MSK parietal cell antibody, and rheumatoid factor, with the response to these tests scored as present or absent.

17.1.3.2 Covariates

Covariates to be used in the immunologic evaluation for adjusted statistical analyses included age, race, military occupation, current alcohol use (drinks/day), lifetime alcohol history (drink-years), current cigarette smoking (cigarettes/day), lifetime cigarette smoking history (pack-years), and exercise history (an index combining both duration and intensity).

Age, race, and military occupation were determined from military records. Lifetime alcohol history was based on information from the 1997 questionnaire and combined with similar information gathered at the 1987 and 1992 follow-up examinations. Each participant was asked about his drinking patterns throughout his lifetime. When a participant's drinking patterns changed, he was asked to describe how his alcohol consumption differed and the duration of time that the drinking pattern lasted. The participant's average daily alcohol consumption was determined for each of the reported drinking pattern periods throughout his lifetime, and an estimate of the corresponding total number of drink-years was derived. One drink-year was the equivalent of drinking 1.5 ounces of an 80-proof alcoholic beverage, one 12-ounce beer, or one 5-ounce glass of wine per day for 1 year. Current alcohol use was defined as the average number of drinks per day during the month prior to completing the questionnaire.

Current cigarette smoking and lifetime cigarette smoking history were based on questionnaire data. For lifetime cigarette smoking history, the respondent's average smoking was estimated over his lifetime based on his responses to the 1997 questionnaire, with 1 pack-year defined as 365 packs of cigarettes smoked during a single year.

A series of questions concerning exercise patterns in the 2 weeks prior to the physical examination were included as part of the 1997 questionnaire. The participants were asked questions on frequency, average duration per frequency, and increase of heart rate or breathing for more than 20 different activities. The answers to these questions were used and combined to determine an index of physical activity incorporating duration and intensity (88, 89), and this covariate was used in adjusted statistical analyses. A participant was classified as active, moderately active, or sedentary based on his responses to the series of questions regarding exercise patterns.

17.1.4 Statistical Methods

Chapter 7, Statistical Methods, describes the basic statistical methods to be used in the immunologic assessment. For the 1985, 1897, and 1992 follow-up studies, large variation was observed from examination group variability. Because of the variation, this covariate generally was incorporated into the unadjusted and the adjusted models of the respective immunologic assessments for the 1985, 1987, and 1992 studies. Plans had been made to use examination group as a covariate in the analysis of the 1997 immunologic data; however, examination group was not significantly associated with immunologic data in the 1997 follow-up study and, consequently, examination group was not used as a covariate in the analyses described in this chapter.

Table 17-2 summarizes the statistical analyses to be performed for the analysis of the immunologic assessment. The first part of this table lists the dependent variables to be analyzed. The second part of the table further describes the covariates to be examined. A covariate was used in its continuous form whenever possible for all adjusted analyses. If the covariate was inherently discrete (e.g., military occupation), or if a categorized form was needed to develop measures of association with the dependent variables, the covariate was categorized as shown in Table 17-2.

Table 17-2. Statistical Analysis for the Immunologic Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Normal Range/ Cutpoints[a]	Covariates[b]	Exclusions[c]	Statistical Analysis and Methods
CD3+ Cells (T Cells) (cells/mm^3)	LAB	C	700–2,400	(1)	(a)	U:GLM A:GLM
CD4+ Cells (Helper T Cells) (cells/mm^3)	LAB	C	400–1,400	(1)	(a)	U:GLM A:GLM
CD8+ Cells (Suppressor Cells) (cells/mm^3)	LAB	C	300–900	(1)	(a)	U:GLM A:GLM
CD16+56+ Cells (Natural Killer Cells) (cells/mm^3)	LAB	C	48–450	(1)	(a)	U:GLM A:GLM
CD20+ Cells (B Cells) (cells/mm^3)	LAB	C	--	(1)	(a)	U:GLM A:GLM
CD3+CD4+ Cells (Helper T Cells) (cells/mm^3)	LAB	C	400–1,400	(1)	(a)	U:GLM A:GLM
Absolute Lymphocytes (cells/mm^3)	LAB	C	1,000–4,800	(1)	(a)	U:GLM A:GLM
IgA (mg/dl)	LAB	C	69–382	(1)	(a)	U:GLM A:GLM
IgG (mg/dl)	LAB	C	723–1,685	(1)	(a)	U:GLM A:GLM
IgM (mg/dl)	LAB	C	63–277	(1)	(a)	U:GLM A:GLM
Lupus Panel: ANA Test	LAB	D	Present Absent	(1)	(a)	U:LR A:LR
Lupus Panel: ANA Thyroid Microsomal Antibody	LAB	D	Present Absent	(1)	(a)	U:LR A:LR

Table 17-2. Statistical Analysis for the Immunologic Assessment (Continued)

Variable (Units)	Data Source	Data Form	Normal Range/ Cutpoints[a]	Covariates[b]	Exclusions[c]	Statistical Analysis and Methods
Lupus Panel: MSK Smooth Muscle Antibody	LAB	D	Present Absent	(1)	(a)	U:LR A:LR
Lupus Panel: MSK Mitochondrial Antibody	LAB	D	Present Absent	(1)	(a)	U:LR,CS A:LR
Lupus Panel: MSK Parietal Antibody	LAB	D	Present Absent	(1)	(a)	U:LR A:LR
Lupus Panel: Rheumatoid Factor	LAB	D	Present Absent	(1)	(a)	U:LR A:LR

[a] Normal ranges are presented for cell surface markers, absolute lymphocytes, and immunoglobulins for reference purposes. Statistical analyses were done only on the continuous form of these dependent variables.

[b] Covariates:
(1): age, race, military occupation, current cigarette smoking, lifetime cigarette smoking history, current alcohol use, lifetime alcohol history, physical activity index.

[c] Exclusions:
(a): participants taking anti-inflammatory (except aspirin and nonsteroidal) or immunosuppression medications, participants testing positive for HIV, participants who recently received x-ray treatment or chemotherapy for cancer.

Covariates

Variable (Units)	Data Source	Data Form	Cutpoints
Age (years)	MIL	D/C	Born≥1942 Born<1942
Race	MIL	D	Black Non-Black
Occupation	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Current Cigarette Smoking (cigarettes/day)	Q-SR	D/C	0-Never 0-Former >0–20 >20
Lifetime Cigarette Smoking History (pack-years)	Q-SR	D/C	0 >0–10 >10
Current Alcohol Use (drinks/day)	Q-SR	D/C	0–1 >1–4 >4

Table 17-2. Statistical Analysis for the Immunologic Assessment (Continued)

Variable (Units)	Data Source	Data Form	Cutpoints
Lifetime Alcohol History (drink-years)	Q-SR	D/C	0 >0–40 >40
Physical Activity Index (kcal/kg/day)	Q-SR	D	Sedentary: <1.45 Moderate: 1.45–<2.95 Very Active: ≥2.95

Abbreviations

Data Source: LAB: 1997 laboratory results
MIL: Air Force military records
Q-SR: Health questionnaires (self-reported)

Data Form: D: Discrete analysis only
C: Continuous analysis only
D/C: Appropriate form for analysis (either discrete or continuous) for covariates

Statistical Analysis: U: Unadjusted analysis
A: Adjusted analysis

Statistical Methods: CS: Chi-square contingency table analysis (continuity-adjusted)
GLM: General linear models analysis
LR: Logistic regression analysis

Table 17-3 provides a summary of participants with missing dependent variable and covariate data. In addition, the number of participants excluded is given. Because approximately 40 percent of the participants were assayed for cell surface markers, Table 17-3 is divided into two parts: (1) a summary for cell surface markers and (2) a summary for absolute lymphocytes, immunoglobulins, and the lupus panel.

Table 17-3. Number of Participants Excluded or with Missing Data for the Immunologic Assessment

		Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
Variable	Variable Use	Ranch Hand	Comparison	Initial	1987	Ranch Hand	Comparison
Cell Surface Markers							
CD20+ Cells (B Cells)	DEP	1	0	1	1	1	0
Current Cigarette Smoking	COV	1	0	0	1	1	0
Lifetime Cigarette Smoking History	COV	2	1	1	2	2	1
Current Alcohol Use	COV	1	0	0	1	1	0
Lifetime Alcohol History	COV	2	0	1	2	2	0
Physical Activity Index	COV	3	3	1	3	3	3

Table 17-3. Number of Participants with Missing Data for the Immunologic Assessment (Continued)

Variable	Variable Use	Group: Ranch Hand	Group: Comparison	Dioxin (Ranch Hands Only): Initial	Dioxin (Ranch Hands Only): 1987	Categorized Dioxin: Ranch Hand	Categorized Dioxin: Comparison
Taking Anti-Inflammatory or Immunosuppressant Medications	EXC	12	12	8	12	12	11
Recent X-ray Treatment or Chemotherapy for Cancer	EXC	10	8	9	10	10	7
HIV Positive	EXC	0	2	0	0	0	2
Absolute Lymphocytes, Immunoglobulins, and Lupus Panel							
Current Cigarette Smoking	COV	1	0	0	1	1	0
Lifetime Cigarette Smoking History	COV	2	1	1	2	2	1
Current Alcohol Use	COV	1	0	0	1	1	0
Lifetime Alcohol History	COV	6	2	3	6	6	1
Physical Activity Index	COV	6	8	2	6	6	8
Taking Anti-Inflammatory or Immunosuppressant Medications	EXC	23	34	14	23	23	32
Recent X-ray Treatment or Chemotherapy for Cancer	EXC	14	17	12	13	13	16
HIV Positive	EXC	3	2	3	3	3	2

Note: DEP = Dependent variable.
COV = Covariate.
EXC = Exclusion.

Cell Surface Markers:
341 Ranch Hands and 477 Comparisons.
192 Ranch Hands for initial dioxin; 339 Ranch Hands for 1987 dioxin.
339 Ranch Hands and 460 Comparisons for categorized dioxin.

Absolute Lymphocytes, Immunoglobulins, and Lupus Panel:
870 Ranch Hands and 1,251 Comparisons.
482 Ranch Hands for initial dioxin; 863 Ranch Hands for 1987 dioxin.
863 Ranch Hands and 1,213 Comparisons for categorized dioxin.

17.2 RESULTS

17.2.1 Dependent Variable-Covariate Associations

Tests of association between the immunologic dependent variables and each of the covariates given in Table 17-2 were conducted. The results are presented in Appendix Table F-9. These associations are pairwise between the dependent variable and the covariate and are not adjusted for any other covariates. Participants taking anti-inflammatory medications, taking immunosuppression medication, testing

positive for HIV, or who have recently received x-ray treatment or chemotherapy for cancer were excluded from all analyses.

The analysis of CD3+ cells (T cells) revealed a significant association with age ($p=0.006$), indicating a decrease in the CD3+ cell count as age increased. A marginally significant association was found between race and CD3+ cell count ($p=0.095$). Blacks displayed a higher mean CD3+ cell count (mean=1,363.1 cells/mm^3) than non-Blacks (mean=1,239.6 cells/mm^3). Analyses also revealed significant associations between CD3+ cell count and current cigarette smoking ($p<0.001$) and between CD3+ cell count and the physical activity index ($p<0.001$). CD3+ cell count increased as the number of cigarettes per day increased and as the activity level decreased.

Tests of association for CD4+ cell (helper T cell) count were significant for age ($p<0.001$), race ($p=0.023$), current cigarette smoking ($p<0.001$), and the physical activity index ($p=0.001$). A marginally significant association was found with lifetime cigarette smoking history ($p=0.053$). The CD4+ cell count decreased with age, and the CD4+ cell count mean was higher for Blacks (mean=958.7 cells/mm^3) than for non-Blacks (mean=844.4 cells/mm^3). As the number of cigarettes per day increased, the CD4+ cell count increased. Participants with the lowest activity level displayed the highest average CD4+ cell counts (mean=889.2 cells/mm^3); the cell count increased as the number of cigarette pack-years increased.

Significant associations with the CD8+ cell (suppressor T cell) count were found for the current cigarette smoking ($p<0.001$) and the physical activity index covariates ($p=0.005$). The CD8+ cell count increased as the number of cigarettes smoked per day increased. The mean CD8+ cell count was highest among those participants classified as sedentary (mean=608.3 cells/mm^3). Participants classified as active displayed the next highest CD8+ cell count mean (mean=548.3 cells/mm^3), followed by those with a moderately active index (mean=539.1 cells/mm^3).

Covariate association tests conducted for the CD16+56+ cell (natural killer cell) count analysis resulted in significant findings for age ($p=0.005$) and current cigarette smoking ($p<0.001$). The CD16+56+ cell count increased as age increased and as the number of cigarettes smoked per day decreased.

Significant covariate associations with the CD20+ cell (B cell) count were found for age ($p<0.001$), race ($p=0.007$), occupation ($p=0.002$), current cigarette smoking ($p<0.001$), current alcohol use ($p=0.007$), and the physical activity index ($p=0.017$). The CD20+ cell count decreased with age, and the CD20+ cell count mean was higher for Blacks (mean=232.9 cells/mm^3) than for non-Blacks (mean=182.2 cells/mm^3). Enlisted groundcrew showed the highest average CD20+ cell count (mean=200.9 cells/mm^3), followed by enlisted flyers (mean=178.8 cells/mm^3) and officers (mean=170.8 cells/mm^3). The CD20+ cell count increased as the number of cigarettes smoked per day increased and as the number of drinks per day decreased. The CD20+ cell count increased as the physical activity level decreased.

Tests of covariate associations with the CD3+CD4+ cell (helper T cell) count were significant for age ($p<0.001$), current cigarette smoking ($p<0.001$), lifetime cigarette smoking history ($p=0.032$), and the physical activity index ($p=0.001$), and marginally significant for race ($p=0.061$). The CD3+CD4+ cell count decreased with age. The mean CD3+CD4+ cell count was higher for Blacks (mean=860.6 cells/mm^3) than for non-Blacks (mean=770.2 cells/mm^3). The CD3+CD4+ cell count increased as current and lifetime cigarette smoking increased. Participants in the sedentary category of the physical activity index showed the highest CD3+CD4+ cell count (mean=814.3 cells/mm^3).

Association tests for absolute lymphocytes revealed significant findings for age ($p<0.001$), occupation ($p<0.001$), current cigarette smoking ($p<0.001$), lifetime cigarette smoking history ($p<0.001$), and the physical activity index ($p<0.001$). The association between absolute lymphocytes and race was

marginally significant (p=0.070). Absolute lymphocytes decreased with age and increased as cigarette smoking increased. Enlisted groundcrew had the highest average absolute lymphocyte count (mean=1,845.8 cells/mm^3), followed by enlisted flyers (mean=1,788.5 cells/mm^3), then officers (mean=1,703.3 cells/mm^3). Blacks displayed a higher mean absolute lymphocyte count (mean=1,879.4 cells/mm^3) than did non-Blacks (mean=1,772.9 cells/mm^3). The least active participants displayed the highest average absolute lymphocyte count (mean=1,831.0 cells/mm^3), compared to those who were moderately active (mean=1,722.7 cells/mm^3) and active (mean=1,719.7 cells/mm^3).

The covariate association analysis for IgA displayed significant findings for age (p=0.012), occupation (p=0.030), and current alcohol use (p=0.032). Marginally significant findings resulted for lifetime alcohol use (p=0.086) and the physical activity index (p=0.088). IgA levels increased with age, current alcohol use, and lifetime alcohol use. Average IgA levels were highest among enlisted groundcrew (mean=238.7 mg/dl), followed by enlisted flyers (mean=237.3 mg/dl), then officers (mean=225.0 mg/dl). Participants with the lowest activity levels displayed the highest mean IgA levels.

Analysis of IgG revealed significant associations with race (p<0.001), occupation (p=0.019), current cigarette smoking (p<0.001), lifetime cigarette smoking (p<0.001), current alcohol use (p<0.001), and lifetime alcohol history (p=0.007). Blacks exhibited a higher average IgG level (mean=1,266.8 mg/dl) than non-Blacks (mean=1,029.2 mg/dl). Enlisted groundcrew exhibited the highest average IgG level (mean=1,058.6 mg/dl) among the occupational strata, followed by enlisted flyers (mean=1,036.8 mg/dl), then officers (mean=1,026.7 mg/dl). IgA levels decreased as current and lifetime cigarette smoking increased and as current and lifetime alcohol use increased.

The covariate analysis of IgM levels revealed significant associations with age (p=0.005), race (p=0.004), and current alcohol use (p=0.010). IgM levels decreased as age increased. Non-Blacks displayed higher average levels of IgM (mean=98.4 mg/dl) as compared to Blacks (mean=85.4 mg/dl). IgM levels increased as the current alcohol use increased.

Tests of association between covariates and ANA revealed a marginally significant relation with age (p=0.098) and significant relations with current cigarette smoking (p=0.001) and lifetime cigarette smoking history (p=0.033). The presence of the ANA was higher among older participants (53.7%) than among younger participants (49.9%). Cigarette smokers who smoke at most 20 cigarettes per day and those with more than 10 pack-years exhibited the greatest percentages of the ANA present (63.2% and 55.1%, respectively).

A marginally significant association between thyroid microsomal antibody and the physical activity index was observed (p=0.061). The highest percentage of participants with the thyroid microsomal antibody present was found in the moderately active category (4.3%), followed by those classified as sedentary (2.9%), then those classified as active (1.7%).

Significant covariate associations for the MSK smooth muscle antibody test included race (p=0.018) and current cigarette smoking (p=0.037). A marginally significant association with the physical activity index was observed (p=0.085). Blacks exhibited a higher presence of the MSK smooth muscle antibody than non-Blacks (19.2% vs. 11.7%, respectively). Cigarette smokers who smoked at most 20 cigarettes per day displayed the highest presence of the smooth muscle antibody (17.2%). Participants categorized as moderately active exhibited the highest presence of the smooth muscle antibody (13.5%), followed by those who were classified as sedentary (12.9%), then those who were active (9.5%).

Tests of covariate association for the MSK mitochondrial antibody revealed a marginally significant association with occupation (p=0.060). Officers had the highest prevalence of the antibody (0.6%), followed by enlisted flyers (0.3%), then enlisted groundcrew (0.0%).

The MSK parietal antibody test displayed a significant covariate association with race (p=0.001). For Blacks, 10.4 percent exhibited the presence of the antibody, as compared to 3.9 percent of non-Blacks.

Association tests for the rheumatoid factor showed age to be marginally significant (p=0.064) and occupation and lifetime cigarette smoking history to be significant (p=0.038 and p=0.006, respectively). The presence of the rheumatoid factor was higher among the older participants (12.2%), compared to a prevalence of 9.5 percent for the younger participants. Enlisted flyers displayed the highest prevalence of a positive rheumatoid factor (13.1%), followed by officers (12.3%), then enlisted groundcrew (9.0%). The heaviest lifetime smokers (in terms of pack-years) showed the highest presence of the rheumatoid factor (12.8%), followed by nonsmokers (11.6%), then moderate lifetime smokers (7.4%).

17.2.2 Exposure Analysis

The following section presents results of the statistical analyses of the dependent variables shown in Table 17-2. Dependent variables were derived from the results of the laboratory portion of the 1997 follow-up examination.

Four models were examined for each dependent variable given in Table 17-2. The analyses of these models are presented below. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7, respectively. These analyses were performed both unadjusted and adjusted for relevant covariates. Model 1 examined the relation between the dependent variable and group (i.e., Ranch Hand or Comparison). In this model, exposure was defined as "yes" for Ranch Hands and "no" for Comparisons without regard to the magnitude of the exposure. As an attempt to quantify exposure, three contrasts of Ranch Hands and Comparisons were performed along with the overall Ranch Hand versus Comparison contrast. These three contrasts compared Ranch Hands and Comparisons within each occupational category (i.e., officers, enlisted flyers, and enlisted groundcrew). As described in previous reports and Table 2-8, the average levels of exposure to dioxin were highest for enlisted groundcrew, followed by enlisted flyers, then officers.

Model 2 explored the relation between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt. If a participant did not have a 1987 dioxin level, the 1992 level was used to estimate the initial dioxin level. If a participant did not have a 1987 or a 1992 dioxin level, the 1997 level was used to estimate the initial dioxin level. A statistical adjustment for the percentage of body fat at the time of the participant's blood measurement of dioxin was included in this model to account for body-fat-related differences in elimination rate (90).

Model 3 divided the Ranch Hands examined in Model 2 into two categories based on their initial dioxin measures. These two categories are referred to as "low Ranch Hand" and "high Ranch Hand." Two additional categories, Ranch Hands with 1987 serum dioxin levels at or below 10 ppt and Comparisons with 1987 serum dioxin levels at or below 10 ppt, were formed and included in the model. Ranch Hands with 1987 serum dioxin levels at or below 10 ppt are referred to as the "background Ranch Hand" category. Dioxin levels in 1992 were used if the 1987 level was not available and dioxin levels in 1997 were used if the 1987 and 1992 levels were not available. These four categories—Comparison, background Ranch Hands, low Ranch Hands, and high Ranch Hands—were used in Model 3 analyses. The relation between the dependent variable in each of the three Ranch Hand categories and the dependent variable in the Comparison category was examined. A fourth contrast, exploring the relation

of the dependent variable in the combined low and high Ranch Hand categories relative to Comparisons, also was conducted. This combination is referred to in the tables as the "low plus high Ranch Hand" category. As in Model 2, a statistical adjustment for the percentage of body fat at the time of the participant's blood measurement of dioxin was included in this model.

Model 4 examined the relation between the dependent variable and 1987 lipid-adjusted dioxin levels in all Ranch Hands with a dioxin measurement. If a participant did not have a 1987 dioxin measurement, the 1992 measurement was used to determine the dioxin level. If a participant did not have a 1987 or a 1992 dioxin measurement, the 1997 measurement was used to determine the dioxin level.

17.2.2.1 Laboratory Variables

17.2.2.1.1 CD3+ Cells (T Cells)

The Model 1 adjusted analysis of CD3+ cells revealed a marginally significant difference in means between Ranch Hands and Comparisons within the enlisted groundcrew stratum (Table 17-4(b): p=0.073, difference of adjusted means=–91.7 cells/mm^3). The mean CD3+ cell count was higher for Comparisons than for Ranch Hands. All other Model 1 contrasts, as well as the Model 2 and Model 3 analyses, were nonsignificant (Table 17-4(a–f): p>0.11 for all analyses).

Results from the Model 4 unadjusted analysis of CD3+ cells were nonsignificant (Table 17-4(g): p=0.316). After adjustment for covariates, a significant and positive association between the 1987 dioxin levels and CD3+ cell count was observed (Table 17-4(h): p=0.046, adjusted slope=0.035). CD3+ cell counts increased as 1987 dioxin levels increased.

Table 17-4. Analysis of CD3+ Cells (T Cells) (cells/mm^3)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***319***	***1,231.0***	***–26.7 --***	***0.431***
	Comparison	***455***	***1,257.7***		
Officer	Ranch Hand	135	1,230.0	39.8 --	0.449
	Comparison	164	1,190.2		
Enlisted Flyer	Ranch Hand	56	1,197.2	–89.6 --	0.270
	Comparison	78	1,286.8		
Enlisted Groundcrew	Ranch Hand	128	1,247.1	–54.2 --	0.308
	Comparison	213	1,301.3		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 17-4. Analysis of CD3+ Cells (T Cells) (cells/mm^3) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	*Ranch Hand*	*316*	*1,245.2*	*–38.5 --*	*0.255*
	Comparison	*451*	*1,283.7*		
Officer	Ranch Hand	134	1,313.3	46.8 --	0.392
	Comparison	162	1,266.5		
Enlisted Flyer	Ranch Hand	56	1,201.6	–96.8 --	0.224
	Comparison	77	1,298.4		
Enlisted Groundcrew	Ranch Hand	126	1,205.6	–91.7 --	0.073
	Comparison	212	1,297.3		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	52	1,163.0	1,166.8	0.013	0.023 (0.023)	0.317
Medium	61	1,288.6	1,285.9			
High	62	1,263.7	1,262.9			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of CD3+ cells versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	52	1,237.6	0.132	0.042 (0.027)	0.113
Medium	60	1,358.6			
High	62	1,388.6			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD3+ cells versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 17-4. Analysis of CD3+ Cells (T Cells) (cells/mm³) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	**n**	**Mean[a]**	**Adj. Mean[ab]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]**	**p-Value[d]**
Comparison	440	1,252.8	1,252.1		
Background RH	142	1,210.4	1,220.8	−31.3 --	0.490
Low RH	84	1,230.2	1,225.9	−26.2 --	0.636
High RH	91	1,251.6	1,242.7	−9.4 --	0.862
Low plus High RH	175	1,241.3	1,234.6	−17.5 --	0.676

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	**n**	**Adj. Mean[a]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]**	**p-Value[c]**
Comparison	436	1,284.8		
Background RH	140	1,237.1	−47.7 --	0.308
Low RH	83	1,272.3	−12.5 --	0.823
High RH	91	1,239.3	−45.5 --	0.403
Low plus High RH	174	1,254.9	−29.9 --	0.474

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 17-4. Analysis of CD3+ Cells (T Cells) (cells/mm^3) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	110	1,196.2	0.003	0.015 (0.015)	0.316
Medium	100	1,216.1			
High	107	1,271.3			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD3+ cells versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	108	1,149.8	0.088	0.035 (0.018)	0.046
Medium	100	1,220.5			
High	106	1,286.6			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD3+ cells versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

17.2.2.1.2 CD4+ Cells (Helper T Cells)

The unadjusted and adjusted analyses of CD4+ cells in Models 1, 2, and 3, as well as the unadjusted analysis in Model 4, were nonsignificant (Table 17-5(a–g): p>0.11 for all analyses). The adjusted analysis of Model 4 revealed a significant and positive association between the 1987 dioxin levels and the CD4+ cell count (Table 17-5(h): p=0.033, adjusted slope=0.038). CD4+ cell counts increased as 1987 dioxin increased.

Table 17-5. Analysis of CD4+ Cells (Helper T Cells) (cells/mm^3)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***319***	***842.0***	***–15.0 --***	***0.511***
	Comparison	***455***	***857.0***		
Officer	Ranch Hand	135	838.0	13.3 --	0.708
	Comparison	164	824.7		
Enlisted Flyer	Ranch Hand	56	808.4	–61.8 --	0.254
	Comparison	78	870.2		
Enlisted Groundcrew	Ranch Hand	128	861.4	–16.5 --	0.646
	Comparison	213	877.9		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***316***	***871.6***	***–22.4 --***	***0.333***
	Comparison	***451***	***894.0***		
Officer	Ranch Hand	134	926.9	20.0 --	0.601
	Comparison	162	906.9		
Enlisted Flyer	Ranch Hand	56	835.6	–61.0 --	0.261
	Comparison	77	896.5		
Enlisted Groundcrew	Ranch Hand	126	842.4	–44.0 --	0.205
	Comparison	212	886.4		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	52	804.2	807.5	0.018	0.027 (0.023)	0.254
Medium	61	883.0	880.6			
High	62	869.6	868.8			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of CD4+ cells versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 17-5. Analysis of CD4+ Cells (Helper T Cells) (cells/mm³) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	52	885.8	0.152	0.041 (0.026)	0.119
Medium	60	961.1			
High	62	967.0			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD4+ cells versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	440	855.4	854.9		
Background RH	142	823.0	830.4	–24.5 --	0.421
Low RH	84	838.7	835.6	–19.3 --	0.605
High RH	91	868.7	862.2	7.3 --	0.842
Low plus High RH	175	854.2	849.3	–5.6 --	0.844

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	436	897.9		
Background RH	140	854.8	–43.1 --	0.176
Low RH	83	893.6	–4.3 --	0.911
High RH	91	886.1	–11.8 --	0.752
Low plus High RH	174	889.7	–8.2 --	0.774

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 17-5. Analysis of CD4+ Cells (Helper T Cells) (cells/mm³) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	110	813.6	0.004	0.017 (0.015)	0.255
Medium	100	825.4			
High	107	882.5			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD4+ cells versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	108	821.6	0.091	0.038 (0.018)	0.033
Medium	100	865.5			
High	106	944.0			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD4+ cells versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

17.2.2.1.3 CD8+ Cells (Suppressor T Cells)

All results from the analyses of CD8+ cells in Models 1 through 4 were nonsignificant (Table 17-6(a–h): p>0.11 for all analyses).

Table 17-6. Analysis of CD8+ Cells (Suppressor T Cells) (cells/mm³)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***319***	***564.5***	***–22.6 --***	***0.254***
	Comparison	***455***	***587.1***		
Officer	Ranch Hand	135	558.7	7.0 --	0.818
	Comparison	164	551.7		
Enlisted Flyer	Ranch Hand	56	563.9	–61.7 --	0.207
	Comparison	78	625.6		
Enlisted Groundcrew	Ranch Hand	128	571.0	–30.7 --	0.319
	Comparison	213	601.7		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 17-6. Analysis of CD8+ Cells (Suppressor T Cells) (cells/mm³) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	**Group**	**n**	**Adjusted Mean[a]**	**Difference of Adj. Means (95% C.I.)[b]**	**p-Value[c]**
All	***Ranch Hand***	***316***	***565.6***	***–27.4 --***	***0.169***
	Comparison	***451***	***593.0***		
Officer	Ranch Hand	134	565.9	7.3 --	0.812
	Comparison	162	558.6		
Enlisted Flyer	Ranch Hand	56	551.8	–72.5 --	0.132
	Comparison	77	624.3		
Enlisted Groundcrew	Ranch Hand	126	564.7	–42.2 --	0.170
	Comparison	212	606.9		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				**Analysis Results for Log_2 (Initial Dioxin)[b]**		
Initial Dioxin	**n**	**Mean[a]**	**Adj. Mean[ab]**	**R^2**	**Slope (Std. Error)[c]**	**p-Value**
Low	52	531.7	531.9	0.001	0.012 (0.029)	0.688
Medium	61	584.9	584.7			
High	62	568.7	568.7			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of CD8+ cells versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)**		
Initial Dioxin	**n**	**Adj. Mean[a]**	**R^2**	**Adj. Slope (Std. Error)[b]**	**p-Value**
Low	52	546.2	0.039	0.023 (0.034)	0.505
Medium	60	608.0			
High	62	609.7			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD8+ cells versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 17-6. Analysis of CD8+ Cells (Suppressor T Cells) (cells/mm^3) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	440	584.2	584.1		
Background RH	142	563.2	565.3	–18.8 --	0.479
Low RH	84	572.7	571.8	–12.3 --	0.706
High RH	91	554.1	552.4	–31.7 --	0.307
Low plus High RH	175	562.9	561.6	–22.5 --	0.355

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	436	592.0		
Background RH	140	576.2	–15.8 --	0.574
Low RH	83	576.2	–15.8 --	0.634
High RH	91	541.9	–50.1 --	0.112
Low plus High RH	174	558.0	–34.0 --	0.164

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 17-6. Analysis of CD8+ Cells (Suppressor T Cells) (cells/mm³) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	110	550.0	0.001	0.009 (0.019)	0.640
Medium	100	571.5			
High	107	569.0			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD8+ cells versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	108	519.5	0.049	0.014 (0.022)	0.540
Medium	100	553.2			
High	106	539.0			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD8+ cells versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

17.2.2.1.4 CD16+56+ Cells (Natural Killer Cells)

The Model 1 unadjusted analysis of CD16+56+ cell count revealed a marginally significant difference between Ranch Hands and Comparisons when examined across all occupational strata (Table 17-7(a): p=0.082, difference of means=–16.6 cells/mm³). In addition, a significant difference among Ranch Hands and Comparisons was found within the enlisted flyer stratum for both the unadjusted and adjusted analyses (Table 17-7(a,b): p=0.018, difference of means=–53.5 cells/mm³; p=0.011, difference of adjusted means=–58.7 cells/mm³). Each analysis displayed a higher CD16+56+ cell count mean for Comparisons. All other Model 1 contrasts and both the unadjusted and adjusted analyses from Model 2 were nonsignificant (Table 17-7(a–d): p>0.10 for all analyses).

Table 17-7. Analysis of CD16+56+ Cells (Natural Killer Cells) (cells/mm³)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***319***	***259.3***	***–16.6 --***	***0.082***
	Comparison	***455***	***275.9***		
Officer	Ranch Hand	135	266.2	–9.9 --	0.521
	Comparison	164	276.1		
Enlisted Flyer	Ranch Hand	56	236.7	–53.5 --	0.018
	Comparison	78	290.2		
Enlisted Groundcrew	Ranch Hand	128	262.4	–8.2 --	0.572
	Comparison	213	270.6		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***316***	***265.8***	***–15.8 --***	***0.106***
	Comparison	***451***	***281.6***		
Officer	Ranch Hand	134	261.0	–10.7 --	0.478
	Comparison	162	271.7		
Enlisted Flyer	Ranch Hand	56	241.8	–58.7 --	0.011
	Comparison	77	300.4		
Enlisted Groundcrew	Ranch Hand	126	280.8	–2.5 --	0.869
	Comparison	212	283.3		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	52	273.6	276.7	0.038	–0.029 (0.032)	0.370
Medium	61	265.1	263.2			
High	62	254.8	254.2			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of CD16+56+ cells versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 17-7. Analysis of CD16+56+ Cells (Natural Killer Cells) (cells/mm³) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	52	265.4	0.112	–0.030 (0.038)	0.429
Medium	60	268.8			
High	62	246.9			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD16+56+ cells versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	440	275.8	275.4		
Background RH	142	254.1	258.9	–16.5 --	0.192
Low RH	84	283.3	281.1	5.7 --	0.726
High RH	91	247.1	243.3	–32.1 --	0.028
Low plus High RH	175	263.9	260.7	–14.7 --	0.209

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	436	282.6		
Background RH	140	268.0	–14.6 --	0.285
Low RH	83	286.7	4.1 --	0.805
High RH	91	252.0	–30.6 --	0.046
Low plus High RH	174	268.0	–14.6 --	0.227

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 17-7. Analysis of CD16+56+ Cells (Natural Killer Cells) (cells/mm³) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	110	258.5	<0.001	0.006 (0.021)	0.772
Medium	100	263.0			
High	107	257.1			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD16+56+ cells versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	108	265.6	0.059	–0.001 (0.025)	0.960
Medium	100	263.8			
High	106	258.6			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD16+56+ cells versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

The results from the Model 3 analysis of CD16+56+ cell count revealed similar results in the unadjusted and adjusted analyses. Comparisons were found to have a significantly higher mean CD16+56+ cell count than Ranch Hands in the high dioxin category in both the unadjusted and adjusted analyses (Table 17-7(e,f): p=0.028, difference of adjusted means=–32.1 cells/mm³; p=0.046, difference of adjusted means=–30.6 cells/mm³, respectively). All other Model 3 contrasts, as well as each analysis for Model 4, were nonsignificant (Table 17-7(e–h): p>0.19 for all analyses).

17.2.2.1.5 CD20+ Cells (B Cells)

All results from the analysis of CD20+ cell count were nonsignificant for Models 1, 3, and 4 (Table 17-8(a,b,e–h): p>0.14 for each analysis). The Model 2 unadjusted analysis revealed a significant and positive association between initial dioxin and CD20+ cell count (Table 17-8(c): p=0.024, slope=0.081). The Model 2 results became marginally significant after adjustment for covariates (Table 17-8(d): p=0.052, adjusted slope=0.075).

Table 17-8. Analysis of CD20+ Cells (B Cells) (cells/mm^3)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***318***	***184.0***	***–1.5 --***	***0.858***
	Comparison	***455***	***185.5***		
Officer	Ranch Hand	134	175.3	8.1 --	0.496
	Comparison	164	167.1		
Enlisted Flyer	Ranch Hand	56	170.2	–15.0 --	0.420
	Comparison	78	185.2		
Enlisted Groundcrew	Ranch Hand	128	200.4	–0.7 --	0.961
	Comparison	213	201.1		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***315***	***196.2***	***–2.0 --***	***0.808***
	Comparison	***451***	***198.2***		
Officer	Ranch Hand	133	211.3	13.1 --	0.343
	Comparison	162	198.2		
Enlisted Flyer	Ranch Hand	56	185.0	–14.7 --	0.450
	Comparison	77	199.7		
Enlisted Groundcrew	Ranch Hand	126	189.2	–10.1 --	0.422
	Comparison	212	199.3		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	51	153.6	154.9	0.052	0.081 (0.035)	0.024
Medium	61	198.4	197.3			
High	62	191.7	191.4			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of CD20+ cells versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 17-8. Analysis of CD20+ Cells (B Cells) (cells/mm^3) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)**		
Initial Dioxin	**n**	**Adj. Mean[a]**	**R^2**	**Adj. Slope (Std. Error)[b]**	**p-Value**
Low	51	203.2	0.236	0.075 (0.038)	0.052
Medium	60	247.8			
High	62	238.9			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD20+ cells versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	**n**	**Mean[a]**	**Adj. Mean[ab]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]**	**p-Value[d]**
Comparison	440	185.0	185.0		
Background RH	142	182.9	183.9	−1.1 --	0.918
Low RH	83	167.1	166.7	−18.3 --	0.141
High RH	91	196.4	195.5	10.5 --	0.419
Low plus High RH	174	181.8	181.1	−3.9 --	0.694

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	**n**	**Adj. Mean[a]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]**	**p-Value[c]**
Comparison	436	198.1		
Background RH	140	200.6	2.5 --	0.827
Low RH	82	185.2	−12.9 --	0.325
High RH	91	194.6	−3.5 --	0.788
Low plus High RH	173	190.1	−8.0 --	0.419

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 17-8. Analysis of CD20+ Cells (B Cells) (cells/mm³) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	110	179.1	0.004	0.026 (0.023)	0.260
Medium	99	170.0			
High	107	197.9			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD20+ cells versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	108	199.9	0.105	0.030 (0.026)	0.253
Medium	99	194.4			
High	106	214.6			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD20+ cells versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

17.2.2.1.6 CD3+CD4+ Cells (Helper T Cells)

All contrasts examined within the CD3+CD4+ cell count analysis of Models 1 and 3 were nonsignificant (Table 17-9(a,b and e,f): p>0.15 for all contrasts). The Model 2 unadjusted analysis of CD3+CD4+ cell count was also nonsignificant (Table 17-9(c): p=0.226), although the adjusted analysis revealed a marginally significant and positive association between initial dioxin and the CD3+CD4+ cell count (Table 17-9(d): p=0.098, adjusted slope=0.046). The Model 4 analysis of CD3+CD4+ cell count was also nonsignificant in the unadjusted analysis (Table 17-9(g): p=0.228) and significant in the adjusted analysis, with a positive association between the 1987 dioxin levels and the CD3+CD4+ cell count (Table 17-9(h): p=0.025, adjusted slope=0.042).

Table 17-9. Analysis of CD3+CD4+ Cells (Helper T Cells) (cells/mm^3)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***319***	***767.4***	***−13.4 --***	***0.541***
	Comparison	***455***	***780.9***		
Officer	Ranch Hand	135	763.1	13.5 --	0.693
	Comparison	164	749.6		
Enlisted Flyer	Ranch Hand	56	737.4	−54.5 --	0.296
	Comparison	78	791.9		
Enlisted Groundcrew	Ranch Hand	128	785.6	−16.1 --	0.641
	Comparison	213	801.8		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***316***	***786.5***	***−20.7 --***	***0.347***
	Comparison	***451***	***807.2***		
Officer	Ranch Hand	134	839.6	19.6 --	0.589
	Comparison	162	820.0		
Enlisted Flyer	Ranch Hand	56	753.7	−53.8 --	0.296
	Comparison	77	807.5		
Enlisted Groundcrew	Ranch Hand	126	758.1	−42.5 --	0.196
	Comparison	212	800.7		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	52	730.7	733.6	0.018	0.030 (0.024)	0.226
Medium	61	807.5	805.4			
High	62	798.1	797.5			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of CD3+CD4+ cells versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 17-9. Analysis of CD3+CD4+ Cells (Helper T Cells) (cells/mm³) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	52	790.9	0.159	0.046 (0.028)	0.098
Medium	60	861.0			
High	62	874.2			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD3+CD4+ cells versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	440	779.1	778.6		
Background RH	142	747.7	753.7	–24.9 --	0.395
Low RH	84	764.0	761.5	–17.1 --	0.632
High RH	91	796.2	790.8	12.2 --	0.731
Low plus High RH	175	780.6	776.6	–2.0 --	0.940

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	436	809.9		
Background RH	140	766.6	–43.3 --	0.151
Low RH	83	806.9	–3.0 --	0.935
High RH	91	803.8	–6.1 --	0.865
Low plus High RH	174	805.3	–4.6 --	0.866

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 17-9. Analysis of CD3+CD4+ Cells (Helper T Cells) (cells/mm^3) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	110	738.7	0.005	0.019 (0.016)	0.228
Medium	100	750.2			
High	107	809.7			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD3+CD4+ cells versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	108	731.1	0.097	0.042 (0.019)	0.025
Medium	100	775.5			
High	106	854.8			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD3+CD4+ cells versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

17.2.2.1.7 Absolute Lymphocytes

All analysis results from Models 1 through 4 for absolute lymphocytes were nonsignificant (Table 17-10(a–h): p>0.10).

Table 17-10. Analysis of Absolute Lymphocytes (cells/mm^3)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***830***	***1,781.2***	***3.2 --***	***0.909***
	Comparison	***1,199***	***1,777.9***		
Officer	Ranch Hand	327	1,730.0	44.8 --	0.292
	Comparison	475	1,685.2		
Enlisted Flyer	Ranch Hand	142	1,753.3	−63.8 --	0.360
	Comparison	178	1,817.2		
Enlisted Groundcrew	Ranch Hand	361	1,840.2	−9.5 --	0.828
	Comparison	546	1,849.6		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 17-10. Analysis of Absolute Lymphocytes (cells/mm^3) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***820***	***1,787.3***	***–6.1 --***	***0.827***
	Comparison	***1,188***	***1,793.3***		
Officer	Ranch Hand	324	1,805.1	52.9 --	0.227
	Comparison	470	1,752.2		
Enlisted Flyer	Ranch Hand	140	1,740.1	–74.3 --	0.279
	Comparison	176	1,814.4		
Enlisted Groundcrew	Ranch Hand	356	1,795.4	–34.6 --	0.412
	Comparison	542	1,830.0		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	148	1,731.1	1,737.8	0.019	0.019 (0.012)	0.121
Medium	152	1,777.4	1,777.7			
High	153	1,838.8	1,831.7			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of absolute lymphocytes versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	148	1,742.9	0.066	0.023 (0.014)	0.109
Medium	150	1,781.8			
High	151	1,837.5			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute lymphocytes versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 17-10. Analysis of Absolute Lymphocytes (cells/mm^3) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,164	1,776.6	1,775.7		
Background RH	371	1,772.5	1,786.3	10.6 --	0.777
Low RH	222	1,757.0	1,752.0	–23.7 --	0.598
High RH	231	1,807.3	1,794.5	18.8 --	0.676
Low plus High RH	453	1,782.5	1,773.5	–2.2 --	0.959

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,154	1,794.7		
Background RH	365	1,821.6	26.9 --	0.477
Low RH	220	1,768.7	–26.0 --	0.562
High RH	229	1,755.8	–38.9 --	0.389
Low plus High RH	449	1,762.1	–32.6 --	0.340

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	281	1,730.6	0.002	0.010 (0.008)	0.222
Medium	271	1,788.5			
High	272	1,817.6			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute lymphocytes versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 17-10. Analysis of Absolute Lymphocytes (cells/mm^3) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	277	1,723.8	0.046	0.008 (0.009)	0.393
Medium	269	1,783.7			
High	268	1,776.6			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute lymphocytes versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

17.2.2.1.8 IgA

Examination of contrasts for Models 1 and 3 in both the unadjusted and adjusted analyses revealed no significant differences in IgA levels between Ranch Hands and Comparisons (Table 17-11(a,b and e,f): p>0.29 for all contrasts). The Model 2 unadjusted analysis of IgA was also nonsignificant (Table 17-11(c): p=0.224), although after adjustment for covariates, the association between initial dioxin and IgA levels was significant and positive (Table 17-11(d): p=0.046, adjusted slope=0.040). The Model 4 unadjusted analysis of IgA revealed a marginally significant and positive association between the 1987 dioxin levels and IgA levels (Table 17-11(g): p=0.051, adjusted slope=0.022), whereas the adjusted Model 4 analysis was nonsignificant (Table 17-11(h): p=0.115).

Table 17-11. Analysis of IgA (mg/dl)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***830***	***232.4***	***–0.9 --***	***0.860***
	Comparison	***1,199***	***233.3***		
Officer	Ranch Hand	327	224.8	–0.4 --	0.958
	Comparison	475	225.2		
Enlisted Flyer	Ranch Hand	142	238.1	1.4 --	0.912
	Comparison	178	236.6		
Enlisted Groundcrew	Ranch Hand	361	237.3	–2.2 --	0.779
	Comparison	546	239.5		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 17-11. Analysis of IgA (mg/dl) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***820***	***234.9***	***–1.4 --***	***0.790***
	Comparison	***1,188***	***236.2***		
Officer	Ranch Hand	324	221.5	–2.5 --	0.740
	Comparison	470	224.0		
Enlisted Flyer	Ranch Hand	140	238.2	0.1 --	0.995
	Comparison	176	238.1		
Enlisted Groundcrew	Ranch Hand	356	246.1	–0.7 --	0.927
	Comparison	542	246.8		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	148	230.8	231.4	0.007	0.021 (0.017)	0.224
Medium	152	241.6	241.6			
High	153	241.1	240.4			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of IgA versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	148	257.2	0.049	0.040 (0.020)	0.046
Medium	150	270.3			
High	151	275.8			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of IgA versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 17-11. Analysis of IgA (mg/dl) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	**n**	**Mean[a]**	**Adj. Mean[ab]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]**	**p-Value[d]**
Comparison	1,164	233.8	233.6		
Background RH	371	225.0	226.8	–6.8 --	0.297
Low RH	222	233.0	232.3	–1.3 --	0.868
High RH	231	242.6	240.9	7.3 --	0.373
Low plus High RH	453	237.8	236.6	3.0 --	0.629

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	**n**	**Adj. Mean[a]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]**	**p-Value[c]**
Comparison	1,154	236.3		
Background RH	365	231.0	–5.3 --	0.435
Low RH	220	233.2	–3.1 --	0.707
High RH	229	241.0	4.7 --	0.575
Low plus High RH	449	237.1	0.8 --	0.890

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin +1)**		
1987 Dioxin	**n**	**Mean[a]**	**R^2**	**Slope (Std. Error)[b]**	**p-Value**
Low	281	221.1	0.005	0.022 (0.011)	0.051
Medium	271	231.1			
High	272	244.7			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of IgA versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 17-11. Analysis of IgA (mg/dl) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	277	240.7	0.031	0.021 (0.013)	0.115
Medium	269	247.3			
High	268	265.1			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of IgA versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

17.2.2.1.9 IgG

All analyses of IgG from Models 1 through 4 were nonsignificant (Table 17-12 (a–h): p>0.21).

Table 17-12. Analysis of IgG (mg/dl)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***830***	***1,035.5***	***–11.8 --***	***0.273***
	Comparison	***1,199***	***1,047.3***		
Officer	Ranch Hand	327	1,022.2	–7.7 --	0.649
	Comparison	475	1,029.8		
Enlisted Flyer	Ranch Hand	142	1,021.8	–27.2 --	0.307
	Comparison	178	1,048.9		
Enlisted Groundcrew	Ranch Hand	361	1,053.3	–8.9 --	0.587
	Comparison	546	1,062.2		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 17-12. Analysis of IgG (mg/dl) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***820***	***1,121.4***	***–13.9 --***	***0.217***
	Comparison	***1,188***	***1,135.4***		
Officer	Ranch Hand	324	1,101.3	–14.3 --	0.417
	Comparison	470	1,115.6		
Enlisted Flyer	Ranch Hand	140	1,111.7	–32.3 --	0.251
	Comparison	176	1,144.1		
Enlisted Groundcrew	Ranch Hand	356	1,145.3	–6.8 --	0.694
	Comparison	542	1,152.2		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	148	1,040.7	1,039.6	0.002	–0.001 (0.009)	0.922
Medium	152	1,061.9	1,061.8			
High	153	1,025.2	1,026.3			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of IgG versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	148	1,132.3	0.119	–0.003 (0.010)	0.761
Medium	150	1,162.9			
High	151	1,107.0			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of IgG versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 17-12. Analysis of IgG (mg/dl) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	**n**	**Mean[a]**	**Adj. Mean[ab]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]**	**p-Value[d]**
Comparison	1,164	1,048.3	1,048.1		
Background RH	371	1,029.2	1,031.9	−16.2 --	0.254
Low RH	222	1,042.7	1,041.7	−6.4 --	0.713
High RH	231	1,042.2	1,039.6	−8.5 --	0.621
Low plus High RH	453	1,042.5	1,040.7	−7.4 --	0.572

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	**n**	**Adj. Mean[a]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]**	**p-Value[c]**
Comparison	1,154	1,136.6		
Background RH	365	1,122.1	−14.5 --	0.340
Low RH	220	1,121.4	−15.2 --	0.404
High RH	229	1,125.1	−11.5 --	0.535
Low plus High RH	449	1,123.3	−13.3 --	0.340

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin +1)**		
1987 Dioxin	**n**	**Mean[a]**	**R^2**	**Slope (Std. Error)[b]**	**p-Value**
Low	281	1,019.6	<0.001	0.002 (0.005)	0.652
Medium	271	1,040.5			
High	272	1,050.1			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of IgG versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 17-12. Analysis of IgG (mg/dl) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	277	1,115.5	0.073	–0.001 (0.006)	0.920
Medium	269	1,132.4			
High	268	1,142.7			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of IgG versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

17.2.2.1.10 IgM

Each result from the analyses of IgM was nonsignificant for Models 1 through 4 (Table 17-13 (a–h): p>0.10 for all analyses).

Table 17-13. Analysis of IgM (mg/dl)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***830***	***96.3***	***–2.1 --***	***0.373***
	Comparison	***1,199***	***98.4***		
Officer	Ranch Hand	327	95.2	–0.6 --	0.862
	Comparison	475	95.9		
Enlisted Flyer	Ranch Hand	142	94.6	–9.7 --	0.102
	Comparison	178	104.4		
Enlisted Groundcrew	Ranch Hand	361	98.0	–0.8 --	0.831
	Comparison	546	98.7		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 17-13. Analysis of IgM (mg/dl) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***820***	***90.5***	***–2.0 --***	***0.365***
	Comparison	***1,188***	***92.4***		
Officer	Ranch Hand	324	89.2	–0.7 --	0.831
	Comparison	470	89.9		
Enlisted Flyer	Ranch Hand	140	89.3	–8.7 --	0.120
	Comparison	176	98.1		
Enlisted Groundcrew	Ranch Hand	356	90.7	–0.7 --	0.824
	Comparison	542	91.4		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for $\log_2$ (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	148	93.9	93.5	0.005	0.007 (0.019)	0.711
Medium	152	96.5	96.5			
High	153	96.0	96.3			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of IgM versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for $\log_2$ (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	148	86.3	0.046	–0.003 (0.022)	0.896
Medium	150	89.7			
High	151	87.9			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of IgM versus $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 17-13. Analysis of IgM (mg/dl) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	**n**	**Mean[a]**	**Adj. Mean[ab]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]**	**p-Value[d]**
Comparison	1,164	98.2	98.2		
Background RH	371	97.1	96.1	–2.1 --	0.487
Low RH	222	95.5	95.8	–2.4 --	0.525
High RH	231	95.5	96.4	–1.8 --	0.619
Low plus High RH	453	95.5	96.1	–2.1 --	0.459

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	**n**	**Adj. Mean[a]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]**	**p-Value[c]**
Comparison	1,154	92.5		
Background RH	365	91.2	–1.3 --	0.659
Low RH	220	90.7	–1.8 --	0.599
High RH	229	89.4	–3.1 --	0.390
Low plus High RH	449	90.0	–2.5 --	0.358

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin +1)**		
1987 Dioxin	**n**	**Mean[a]**	**R^2**	**Slope (Std. Error)[b]**	**p-Value**
Low	281	96.4	<0.001	–0.001 (0.012)	0.937
Medium	271	96.4			
High	272	95.7			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of IgM versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 17-13. Analysis of IgM (mg/dl) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	277	88.6	0.025	–0.008 (0.014)	0.586
Medium	269	89.3			
High	268	86.4			

[a] Transformed from natural logarithm scale
[b] Slope and standard error based on natural logarithm of IgM versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

17.2.2.1.11 Lupus Panel: ANA Test

All analysis results from Models 1 through 4 for the antinuclear antibody were nonsignificant (Table 17-14(a–h): p>0.20).

Table 17-14. Analysis of Lupus Panel: ANA Test

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Present	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***830***	***432 (52.1)***	***1.00 (0.84,1.19)***	***0.998***
	Comparison	***1,199***	***624 (52.0)***		
Officer	Ranch Hand	327	168 (51.4)	0.94 (0.71,1.25)	0.683
	Comparison	475	251 (52.8)		
Enlisted Flyer	Ranch Hand	142	73 (51.4)	1.11 (0.71,1.72)	0.653
	Comparison	178	87 (48.9)		
Enlisted Groundcrew	Ranch Hand	361	191 (52.9)	1.02 (0.78,1.33)	0.876
	Comparison	546	286 (52.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.01 (0.84,1.20)***	***0.946***
Officer	0.95 (0.72,1.27)	0.736
Enlisted Flyer	1.07 (0.68,1.67)	0.778
Enlisted Groundcrew	1.04 (0.79,1.36)	0.801

Table 17-14. Analysis of Lupus Panel: ANA Test (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Present	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	148	76 (51.4)	1.08 (0.94,1.24)	0.301
Medium	152	71 (46.7)		
High	153	85 (55.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
449	1.04 (0.88,1.24)	0.622

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Present	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,164	606 (52.1)		
Background RH	371	199 (53.6)	1.05 (0.83,1.33)	0.674
Low RH	222	105 (47.3)	0.83 (0.62,1.11)	0.202
High RH	231	127 (55.0)	1.14 (0.85,1.51)	0.380
Low plus High RH	453	232 (51.2)	0.97 (0.78,1.21)	0.810

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,154		
Background RH	365	1.04 (0.82,1.33)	0.738
Low RH	220	0.85 (0.63,1.14)	0.276
High RH	229	1.15 (0.85,1.55)	0.364
Low plus High RH	449	0.99 (0.79,1.24)	0.936

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 17-14. Analysis of Lupus Panel: ANA Test (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Present	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	281	153 (54.5)	0.98 (0.90,1.08)	0.732
Medium	271	134 (49.5)		
High	272	144 (52.9)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
814	0.96 (0.86,1.08)	0.512

[a] Relative risk for a twofold increase in 1987 dioxin.

17.2.2.1.12 Lupus Panel: Thyroid Microsomal Antibody

All results from the analyses of the thyroid microsomal antibody from Models 1 through 4 were nonsignificant (Table 17-15(a–h): p>0.27).

Table 17-15. Analysis of Lupus Panel: ANA Thyroid Microsomal Antibody

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Present	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***830***	***24 (2.9)***	***1.02 (0.60,1.73)***	***0.941***
	Comparison	***1,199***	***34 (2.8)***		
Officer	Ranch Hand	327	11 (3.4)	1.15 (0.51,2.56)	0.739
	Comparison	475	14 (3.0)		
Enlisted Flyer	Ranch Hand	142	3 (2.1)	0.75 (0.18,3.18)	0.693
	Comparison	178	5 (2.8)		
Enlisted Groundcrew	Ranch Hand	361	10 (2.8)	1.01 (0.45,2.27)	0.984
	Comparison	546	15 (2.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.02 (0.59,1.75)***	***0.947***
Officer	1.14 (0.51,2.55)	0.750
Enlisted Flyer	0.75 (0.17,3.19)	0.692
Enlisted Groundcrew	1.00 (0.43,2.35)	0.994

Table 17-15. Analysis of Lupus Panel: ANA Thyroid Microsomal Antibody (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Present	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	148	6 (4.1)	0.77 (0.47,1.26)	0.272
Medium	152	3 (2.0)		
High	153	3 (2.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
449	0.77 (0.43,1.35)	0.344

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Present	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,164	34 (2.9)		
Background RH	371	12 (3.2)	1.13 (0.58,2.22)	0.717
Low RH	222	7 (3.2)	1.08 (0.47,2.46)	0.862
High RH	231	5 (2.2)	0.72 (0.28,1.88)	0.506
Low plus High RH	453	12 (2.7)	0.88 (0.45,1.73)	0.709

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 17-15. Analysis of Lupus Panel: ANA Thyroid Microsomal Antibody (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,154		
Background RH	365	1.03 (0.51,2.12)	0.925
Low RH	220	1.12 (0.49,2.59)	0.785
High RH	229	0.81 (0.30,2.16)	0.671
Low plus High RH	449	0.95 (0.48,1.90)	0.883

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Present	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	281	8 (2.9)	0.90 (0.68,1.20)	0.486
Medium	271	10 (3.7)		
High	272	6 (2.2)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
814	0.96 (0.69,1.35)	0.824

[a] Relative risk for a twofold increase in 1987 dioxin.

17.2.2.1.13 Lupus Panel: MSK Smooth Muscle Antibody

The Model 1 analysis revealed a significant difference in the presence of the MSK smooth muscle antibody between Ranch Hands (8.5%) and Comparisons (16.3%) in the enlisted flyer stratum. The analyses were significant both unadjusted and adjusted for covariates (Table 17-16(a,b): p=0.040, Est. RR=0.47; p=0.045, Adj. RR=0.48, respectively). All other Model 1 contrasts were nonsignificant (Table 17-16(a,b): p>0.21).

Table 17-16. Analysis of Lupus Panel: MSK Smooth Muscle Antibody

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Present	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***830***	***101 (12.2)***	***1.01 (0.77,1.32)***	***0.959***
	Comparison	***1,199***	***145 (12.1)***		
Officer	Ranch Hand	327	43 (13.2)	1.32 (0.85,2.04)	0.217
	Comparison	475	49 (10.3)		
Enlisted Flyer	Ranch Hand	142	12 (8.5)	0.47 (0.23,0.97)	0.040
	Comparison	178	29 (16.3)		
Enlisted Groundcrew	Ranch Hand	361	46 (12.7)	1.04 (0.70,1.56)	0.833
	Comparison	546	67 (12.3)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.99 (0.75,1.31)***	***0.953***
Officer	1.30 (0.84,2.03)	0.239
Enlisted Flyer	0.48 (0.24,0.99)	0.045
Enlisted Groundcrew	1.02 (0.68,1.53)	0.934

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Present	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	148	18 (12.2)	0.80 (0.62,1.02)	0.061
Medium	152	20 (13.2)		
High	153	11 (7.2)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
449	0.77 (0.58,1.04)	0.082

[a] Relative risk for a twofold increase in initial dioxin.

Table 17-16. Analysis of Lupus Panel: MSK Smooth Muscle Antibody (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	**n**	**Number (%) Present**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,164	141 (12.1)		
Background RH	371	52 (14.0)	1.23 (0.87,1.74)	0.235
Low RH	222	30 (13.5)	1.12 (0.73,1.71)	0.601
High RH	231	19 (8.2)	0.63 (0.38,1.04)	0.071
Low plus High RH	453	49 (10.8)	0.83 (0.59,1.19)	0.315

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Comparison	1,154		
Background RH	365	1.28 (0.90,1.83)	0.173
Low RH	220	1.07 (0.70,1.65)	0.752
High RH	229	0.59 (0.36,1.00)	0.048
Low plus High RH	449	0.79 (0.55,1.14)	0.209

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**	
1987 Dioxin	**n**	**Number (%) Present**	**Estimated Relative Risk (95% C.I.)[a]**	**p-Value**
Low	281	34 (12.1)	0.88 (0.76,1.02)	0.087
Medium	271	38 (14.0)		
High	272	29 (10.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 17-16. Analysis of Lupus Panel: MSK Smooth Muscle Antibody (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
814	0.89 (0.75,1.05)	0.155

[a] Relative risk for a twofold increase in 1987 dioxin.

A marginally significant and inverse association was found between initial dioxin and the presence of the MSK smooth muscle antibody in both the unadjusted and adjusted analyses of Model 2 (Table 17-16(c,d): p=0.061, Est. RR=0.80; p=0.082, Adj. RR=0.77, respectively). As initial dioxin increased, the percentage of Ranch Hands with the MSK smooth muscle antibody present decreased.

The unadjusted analysis of Model 3 uncovered a marginally significant difference in the presence of the MSK smooth muscle antibody between Ranch Hands in the high dioxin category (8.2%) and Comparisons (12.1%) (Table 17-16(e): p=0.071, Est. RR=0.63). After adjustment for covariates, the association became significant (Table 17-16(f): p=0.048, Adj. RR=0.59). All other Model 3 contrasts were nonsignificant in both unadjusted and adjusted analyses (Table 17-16(e,f): p>0.17 for all contrasts).

The Model 4 unadjusted analysis revealed a marginally significant association between the 1987 dioxin levels and the presence of the MSK smooth muscle antibody (Table 17-16(g): p=0.087, Est. RR=0.88). After adjustment for covariates, the association was nonsignificant (Table 17-16(h): p=0.155).

17.2.2.1.14 Lupus Panel: MSK Mitochondrial Antibody

Due to the sparseness of the presence of the MSK mitochondrial antibody among the study participants, analyses were limited. The Model 1 adjusted analysis of MSK mitochondrial antibody displayed a marginally significant difference in the presence of the antibody between Ranch Hands (1.2%) and Comparisons (0.2%) in the officer stratum (Table 17-17(b): p=0.098, Adj. RR=6.58). All other Model 1 analyses performed were nonsignificant (Table 17-17(a,b): p>0.11).

Table 17-17. Analysis of Lupus Panel: MSK Mitochondrial Antibody

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Present	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***830***	***4 (0.5)***	***2.90 (0.53,15.86)***	***0.203***
	Comparison	***1,199***	***2 (0.2)***		
Officer	Ranch Hand	327	4 (1.2)	5.87 (0.65,52.76)	0.114
	Comparison	475	1 (0.2)		
Enlisted Flyer	Ranch Hand	142	0 (0.0)	--	0.999[a]
	Comparison	178	1 (0.6)		
Enlisted Groundcrew	Ranch Hand	361	0 (0.0)	--	--
	Comparison	546	0 (0.0)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with the MSK mitochondrial antibody present.

--: Results not presented because of the sparse number of participants with the MSK mitochondrial antibody present.

Table 17-17. Analysis of Lupus Panel: MSK Mitochondrial Antibody (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	**Adjusted Relative Risk (95% C.I.)**	**p-Value**
All	*2.79 (0.51,15.31)*	*0.222*
Officer	6.58 (0.70,61.53)	0.098
Enlisted Flyer	--	--
Enlisted Groundcrew	--	--

--: Results not presented because of the sparse number of participants with the MSK mitochondrial antibody present.

Note: Results are not adjusted for race, occupation (contrast of all Ranch Hands with all Comparisons), current alcohol use, and physical activity index because of the sparse number of participants with the MSK mitochondrial antibody present.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)**[a]	
Initial Dioxin	**n**	**Number (%) Present**	**Estimated Relative Risk (95% C.I.)**[b]	**p-Value**
Low	148	2 (1.4)	0.11 (0.01,4.01)	0.034
Medium	152	0 (0.0)		
High	153	0 (0.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)**[a]	**p-Value**
450	0.10 (0.01,4.01)	0.049

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race, current alcohol use, and physical activity index due to the sparse number of participants with the MSK mitochondrial antibody present.

Table 17-17. Analysis of Lupus Panel: MSK Mitochondrial Antibody (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Present	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,164	2 (0.2)		
Background RH	371	2 (0.5)	3.74 (0.51,27.25)	0.193
Low RH	222	2 (0.9)	4.91 (0.68,35.44)	0.114
High RH	231	0 (0.0)	--	0.999[c]
Low plus High RH	453	2 (0.4)	--	0.672[c]

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with the MSK mitochondrial antibody present.
--: Results not presented because of the sparse number of participants with the MSK mitochondrial antibody present.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,154		
Background RH	365	3.55 (0.48,26.04)	0.213
Low RH	220	4.30 (0.57,32.27)	0.156
High RH	229	--	--
Low plus High RH	449	--	--

[a] Relative risk and confidence interval relative to Comparisons.
--: Results not presented because of the sparse number of participants with the MSK mitochondrial antibody present.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for race, occupation, current alcohol, and physical activity index because of the sparse number of participants with the MSK mitochondrial antibody present.

Table 17-17. Analysis of Lupus Panel: MSK Mitochondrial Antibody (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Present	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	281	1 (0.4)	0.62 (0.29,1.33)	0.206
Medium	271	3 (1.1)		
High	272	0 (0.0)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
814	0.65 (0.31,1.37)	0.245

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race, occupation, current alcohol, and physical activity index because of the sparse number of participants with the MSK mitochondrial antibody present.

The Model 2 analysis of MSK mitochondrial antibody showed a significant inverse association with initial dioxin (Est. RR=0.11, p=0.034, unadjusted; Adj. RR=0.10, p=0.049, adjusted). The percentage of participants with MSK mitochondrial antibody increased as initial dioxin decreased.

All Model 3 and 4 analyses were nonsignificant (Table 17-17 (e,h): p>0.11).

17.2.2.1.15 Lupus Panel: MSK Parietal Antibody

The Model 1 unadjusted and adjusted analyses of the MSK parietal antibody found no significant differences between Ranch Hands and Comparisons examined across all occupations and within each occupational stratum (Table 17-18(a,b): p>0.33). Results were also nonsignificant for the Model 2 and 4 analyses of MSK parietal antibody (Table 17-18(c,d and g,h): p≥0.14).

Table 17-18. Analysis of Lupus Panel: MSK Parietal Antibody

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Present	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***830***	***36 (4.3)***	***1.02 (0.66,1.58)***	***0.927***
	Comparison	***1,199***	***51 (4.3)***		
Officer	Ranch Hand	327	14 (4.3)	1.37 (0.65,2.88)	0.404
	Comparison	475	15 (3.2)		
Enlisted Flyer	Ranch Hand	142	5 (3.5)	0.61 (0.20,1.84)	0.382
	Comparison	178	10 (5.6)		
Enlisted Groundcrew	Ranch Hand	361	17 (4.7)	0.99 (0.53,1.85)	0.971
	Comparison	546	26 (4.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.00 (0.64,1.56)***	***0.996***
Officer	1.36 (0.65,2.87)	0.416
Enlisted Flyer	0.58 (0.19,1.74)	0.331
Enlisted Groundcrew	0.97 (0.51,1.85)	0.920

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Present	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	148	10 (6.8)	0.86 (0.63,1.18)	0.335
Medium	152	10 (6.6)		
High	153	6 (3.9)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
449	0.93 (0.64,1.35)	0.694

[a] Relative risk for a twofold increase in initial dioxin.

Table 17-18. Analysis of Lupus Panel: MSK Parietal Antibody (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	**n**	**Number (%) Present**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,164	50 (4.3)		
Background RH	371	9 (2.4)	0.61 (0.29,1.25)	0.179
Low RH	222	16 (7.2)	1.68 (0.94,3.02)	0.082
High RH	231	10 (4.3)	0.93 (0.46,1.87)	0.843
Low plus High RH	453	26 (5.7)	1.24 (0.75,2.05)	0.392

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Comparison	1,154		
Background RH	365	0.63 (0.30,1.31)	0.216
Low RH	220	1.50 (0.82,2.75)	0.192
High RH	229	0.97 (0.47,1.99)	0.928
Low plus High RH	449	1.20 (0.72,2.00)	0.490

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**	
1987 Dioxin	**n**	**Number (%) Present**	**Estimated Relative Risk (95% C.I.)[a]**	**p-Value**
Low	281	6 (2.1)	1.14 (0.92,1.42)	0.245
Medium	271	15 (5.5)		
High	272	14 (5.2)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 17-18. Analysis of Lupus Panel: MSK Parietal Antibody (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
814	1.22 (0.93,1.60)	0.140

[a] Relative risk for a twofold increase in 1987 dioxin.

The unadjusted analysis for Model 3 revealed a marginally significant difference in the presence of the MSK parietal antibody among Ranch Hands in the low dioxin category and Comparisons (Table 17-18(e): p=0.082, Est. RR=1.68). The percentage of participants with the MSK parietal antibody present was 7.2 among Ranch Hands in the low dioxin category and 4.3 for Comparisons. After adjustment for covariates, the difference between Ranch Hands in the low dioxin category and Comparisons was nonsignificant (Table 17-18(f): p=0.192). All other Model 3 contrasts were nonsignificant (Table 17-18(e,f): p>0.17).

17.2.2.1.16 Lupus Panel: Rheumatoid Factor

All Model 1 unadjusted and adjusted contrasts examining the presence of a positive rheumatoid factor among Ranch Hands and Comparisons were nonsignificant (Table 17-19(a,b): p>0.16).

Table 17-19. Analysis of Lupus Panel: Rheumatoid Factor

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Present	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***830***	***89 (10.7)***	***0.95 (0.72,1.27)***	***0.748***
	Comparison	***1,199***	***134 (11.2)***		
Officer	Ranch Hand	327	43 (13.2)	1.13 (0.74,1.73)	0.565
	Comparison	475	56 (11.8)		
Enlisted Flyer	Ranch Hand	142	19 (13.4)	1.04 (0.54,2.00)	0.904
	Comparison	178	23 (12.9)		
Enlisted Groundcrew	Ranch Hand	361	27 (7.5)	0.72 (0.45,1.17)	0.184
	Comparison	546	55 (10.1)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.91 (0.69,1.22)***	***0.540***
Officer	1.09 (0.71,1.68)	0.692
Enlisted Flyer	0.98 (0.51,1.91)	0.956
Enlisted Groundcrew	0.71 (0.44,1.15)	0.167

Table 17-19. Analysis of Lupus Panel: Rheumatoid Factor (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Present	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	148	15 (10.1)	0.75 (0.57,0.99)	0.033
Medium	152	17 (11.2)		
High	153	10 (6.5)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
449	0.83 (0.60,1.14)	0.233

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Present	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,164	130 (11.2)		
Background RH	371	46 (12.4)	1.15 (0.80,1.65)	0.458
Low RH	222	27 (12.2)	1.10 (0.70,1.70)	0.686
High RH	231	15 (6.5)	0.54 (0.31,0.95)	0.032
Low plus High RH	453	42 (9.3)	0.77 (0.52,1.12)	0.170

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 17-19. Analysis of Lupus Panel: Rheumatoid Factor (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,154		
Background RH	365	1.04 (0.71,1.51)	0.841
Low RH	220	1.03 (0.66,1.61)	0.890
High RH	229	0.59 (0.33,1.04)	0.068
Low plus High RH	449	0.77 (0.53,1.14)	0.195

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Present	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	281	36 (12.8)	0.81 (0.69,0.96)	0.010
Medium	271	33 (12.2)		
High	272	19 (7.0)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
814	0.86 (0.71,1.04)	0.122

[a] Relative risk for a twofold increase in 1987 dioxin.

A significant inverse association between initial dioxin and the presence of a positive rheumatoid factor was found from the Model 2 unadjusted analysis (Table 17-19(c): p=0.033, Est. RR=0.75). After adjustment for covariates, the association became nonsignificant (Table 17-19(d): p=0.233).

The Model 3 unadjusted analysis displayed a significant difference in the percentage of positive rheumatoid factors among Ranch Hands in the high dioxin category (6.5%) and Comparisons (11.2%) (Table 17-19(e): p=0.032, Est. RR=0.54). After adjustment for covariates, the difference was marginally significant (Table 17-19(f): p=0.068, Adj. RR=0.59). All other unadjusted and adjusted Model 3 contrasts were nonsignificant (Table 17-19(e,f): p≥0.17).

A significant inverse association between the 1987 dioxin levels and the presence of a positive rheumatoid factor was found in the Model 4 unadjusted analysis (Table 17-19(g): p=0.010, Est. RR=0.81). After adjustment for covariates, the association was nonsignificant (Table 17-19(h): p=0.122).

17.3 DISCUSSION

Immunologic competence was assessed by a combination of laboratory assays on blood samples that examined lymphocyte surface markers on a randomized subset of the study population, immunoglobulin quantitation, and autoantibodies.

Evaluation of the human immune system is divided into two separate segments: humoral and cellular immunity. Circulating in the plasma phase of blood, the humoral segment consists of the immunoglobulins and complement proteins (complement C3 and C4 analysis presented in Chapter 13, Gastrointestinal Assessment). Some immunoglobulins (especially IgA) are prominent at exposed sites of the body (e.g., the mucosal surfaces of the mouth, pulmonary tract, and gastrointestinal tract), where direct contact with microorganisms is frequent. The serum immunoglobulins are secreted by plasma cells within the bone marrow through a process regulated in a sequence of events modulated by macrophages and memory lymphocytes. The immunoglobulins serve as a defense against bacterial infections, the bloodborne phase of viral infections, and in many other situations when microorganisms invade the body.

Quantitation of the immunoglobulins IgG, IgA, and IgM in serum gives an overall view of B cell integrity when related to the expected reference range values found in a normal, healthy population. Selective deficiency of one or more of these antibody classes, whether congenital or acquired, may be associated with increased susceptibility to infections (e.g., pneumonia). Congenital deficiencies are usually clinically evident early in life due to a large number of infections frequently resulting in death in childhood. Acquired deficiencies of immunoglobulins can occur in leukemias and lymphomas that invade the bone marrow later in adult life. Elevations of these immunoglobulins in a polyclonal pattern are frequently an indication of chronic infections (perhaps as compensation for the impairment of another segment of the immune response), of chronic inflammation such as in autoimmune disease, or of faulty regulation of B cell responses such as occurs in hepatic cirrhosis. Thus, measurement of immunoglobulins in serum yields clinical information relevant to past immunologic stimulation from infections, potential to defend the body against further infectious challenges, and the functional capacity of the liver in chronic disease.

Further evidence for the integrity of the immune system in aging individuals is the presence or absence of various autoantibodies. The autoantibodies measured in the lupus panel are considered to be abnormalities when present. Although autoantibodies often demonstrate an association with specific diseases that is useful in diagnosing and monitoring those diseases, sometimes the same autoantibodies can be found as isolated laboratory abnormalities in otherwise healthy individuals. In those cases, autoantibodies may be interpreted almost as renegade substances deriving from an aging and faltering immune system, and as such are markers for deterioration of the B cell regulatory process of immunity.

The second segment, cellular immunity, consists of both granulocytic and lymphocytic processes. Abnormalities of granulocytes can frequently be discerned from examination of the peripheral blood smear as part of the complete blood count. In addition, the medical history of individuals is usually sufficient to ascertain whether granulocyte deficiency is a consideration. Chapter 16, Hematologic Assessment, discusses the effect of dioxin on the components of these cells.

The total number of circulating lymphocytes (also called absolute number) provides information relative to the basic cellular quantity of cells present and available in the body for mounting an immune response. An increase in the total number of lymphocytes is observed in lymphocytic leukemias; it may also occur as a defensive immune response to some acute infections. Deficiency in the total number of lymphocytes may indicate susceptibility to infections with viruses or fungi. The total number of lymphocytes is usually decreased in malnutrition, often leading to infections in malnourished persons.

Examination of marker proteins on the surfaces of lymphocytes by flow cytometry is an excellent means of evaluating whether the regulatory interactions between the subpopulations of T cells, B cells, and monocytes are intact. An alteration in the percentages of any of these categories of cells can be considered presumptive evidence of an inability to recognize and destroy foreign infectious agents or tumor cells. The marker for total T cells was CD3+; the T cells were further broken down into the subpopulations of CD4+ (helper cells) and CD8+ (suppressor cells). The body's ability to respond to infectious challenges decreases in proportion to depression of the CD4+ count. This relation is particularly important in patients with AIDS because the HIV directly infects and destroys CD4+ lymphocytes, thereby incapacitating the immune system leading to infections with opportunistic organisms that normally would not cause infections in humans. The CD4+ count is also depressed by immunosuppressive medications such as cyclosporine, which are used to prevent rejection of organ transplants (e.g., kidney, heart). Immunosuppressed persons have a higher rate of malignancies, presumably in part because of diminished capacity of the immune system to search for and destroy tumor cells. The CD16+56+ markers are found on natural killer lymphocytes that provide a strong line of defense against growth of neoplasms through their action of destroying target cells by antibody-dependent, complement-mediated cytolysis. Changes in the mean number of CD16+56+ cells (natural killer cells) should not be over interpreted. Scientists know very little about the clinical significance of these cells; some authors suggest that these cells alter during times of stress. Occasionally, there has been a case report of patients who lack these cells. In general, the natural killer cell population is heterogeneous and the role of these cells in humans is unknown. CD20+ is a surface marker for B cells and gives an indication of the balance between cellular immunity and the ability to mount a B cell response with production of specific antibodies.

Interpretation of alterations in the relative amounts of B cells, T cells, their subsets, and monocytes is based on the expectation that all aspects of the immune system must be intact to prevent infections and to guard against development of tumors with unusual surface antigens. The antibodies specific for tumors can either help to destroy them by binding complement and lysing the cells or stabilize them if those antibodies attach to the tumor surface without binding complement, thereby blocking immune recognition and destruction of tumor cells. The T cells also have antigen receptors on their surfaces that similarly call into play the destructive power of the entire lymphocyte cell line in an antitumor attack. T cells stimulated by interleukin-2 have even greater capacity to attack and destroy foreign antigens and tumors by the other recognition factors such as antibodies and complement proteins.

The immunologic evaluation performed on AFHS participants went far beyond the usual medical examinations employed for general health assessments. As a test panel battery, this assessment provided an in-depth, broad review of immunologic parameters designed to detect abnormalities or variances that may or may not carry clinical import. In fact, the choice of all these sensitive laboratory tests may make it statistically possible to detect some subtle effect of dioxin on the immune system.

This thorough evaluation of the immune system did not reveal any relations between dioxin exposure and clinically overt disease, but unknown subclinical effects of dioxin on the immune system cannot be ruled out. Some individual elements showed statistical significance, although the magnitude of such relations was small and certainly not to be interpreted as conveying health risk. These included the following

associations with increasing dioxin level: a slight increase in CD3+ cells (T cells), a slight increase in CD4+ cells (helper T cells), a slight decrease in CD16+56+ cells (natural killer cells), and a slight increase in CD20+ cells (B cells). These combinations of results do not necessarily indicate a disorder, and the magnitude of each effect in itself is not considered clinically meaningful. The difference in the magnitude of absolute lymphocytes between the 1992 examination (the mean was approximately 1,940 cells/mm^3) versus the 1997 examination (the mean was approximately 1,780 cells/mm^3) was caused by an equipment upgrade from the Coulter STKR® in 1992 to the Coulter STKS® in 1997. The Coulter STKS® had a slightly lower reference range than the Coulter STKR®.

In the 1997 study, approximately 50 percent of both Ranch Hand and Comparison participants exhibited positive results on the ANA test. This positive rate was much higher than expected for an adult male population. The ANA positive rate also was significantly higher in the 1997 study than in the 1992 study, when about 15 percent of both Ranch Hand and Comparison groups were positive. A shift in the sensitivity of detection for ANA may have occurred from the 1992 study to the 1997 study. In 1997, all ANA tests were read by the same dedicated technologist. For the last several months of the study, the tests also were backread by an expert reviewer who verified all positive results. This quality control procedure guaranteed that the technique for detection was consistent and accurate in the 1997 study. ANA is a screening test done at a particular dilution of serum, typically 1:40. Samples that screen positive are then titered to endpoint (1:80, 1:160, etc.) and a pattern (e.g., homogeneous, speckled, nucleolar, centromere) is identified. Most laboratory clinicians screen at 1:40 and report results that are less than or equal to 1:160 as "indeterminate" or "borderline." Borderline ANA test results rarely are clinically important (significant). The clinician decides whether the result is clinically important and whether to do follow-up tests for more specific antinuclear antibodies. Results of 1:320 or greater are considered positive; the higher the titer, the more likely it is to be clinically significant.

The screening dilution (1:40 in the AFHS) usually is determined by the laboratory to be that concentration at which 95 percent of normal individuals are negative. As humans age, it is well recognized that the percentage of normal asymptomatic individuals who screen positive increases. It is not practical to adjust screening dilutions by age; therefore, screening at a dilution of 1:40 is used for all individuals—regardless of their age—knowing that there will be more false positives as age increases. Clinicians usually take that into consideration when interpreting the low level positives and borderline results.

In the AFHS, the ANA test was scored as positive or negative. The percentage positive in the Comparison group is more than 5 percent, as it was in the last report, for two reasons: (1) it does not distinguish trivial positives from serious positives and (2) the population is getting older. Unfortunately, readers lacking knowledge of the test may interpret this as a Vietnam effect, when in fact the increase is more likely due to aging and lack of resolution of the degree of abnormality. In future studies, the degree of abnormality will be scored.

An inverse relation was found between dioxin exposure and the presence of autoantibodies against MSK smooth muscle. Other autoantibodies examined (ANA in the lupus panel and rheumatoid factor) did not show a relation with dioxin in the 1997 follow-up study, although they had previously done so in the 1992 follow-up examination. The Comparison group showed a rate of abnormal (positive) results for smooth muscle autoantibody that is expected in a general population. As in the 1992 follow-up study, the Ranch Hand group actually had a lower number of abnormal results for the smooth muscle autoantibody than did the Comparison group. This statistically negative association may indicate a highly sensitive but not clinically meaningful first indication of a generalized immune suppression, because a certain percentage of normal individuals should have been expected to test positive but did not. Clarification of the relevance of these findings to a hypothesis of dioxin-induced immune suppression will require longitudinal analysis of data from future physical examinations.

Serum IgA concentrations increased significantly with initial dioxin. IgA means were not significantly increased in Ranch Hand enlisted groundcrew or in the high dioxin category and IgA did not increase significantly with 1987 dioxin. Similar results were observed in 1992 and in 1987. In 1992, significant increases in IgA with initial dioxin were noted; there were no corresponding increases in Ranch Hand enlisted groundcrew or in the high dioxin category. IgA was not significantly related with 1987 dioxin. In 1987, IgA increased significantly with initial dioxin, but was not significantly increased in the high dioxin category; the Ranch Hand and Comparison IgA means were not significantly different and analyses restricted to enlisted groundcrew were not conducted. IgA was not measured in 1982 and 1985. These results, although significant, were small in magnitude and their clinical significance is unknown.

In many instances, statistical correlations existed between immunologic parameters and the covariates age, tobacco use, alcohol consumption, and exercise. Consequently, it is important to account for this potential source of variation between Ranch Hands and Comparisons. The analysis of covariate associations with immunologic variables yielded strong findings, especially with regard to current and lifetime cigarette smoking. Recent work has demonstrated the particular effect of tobacco use on the immune response (53–57). Current and lifetime alcohol use showed some mild associations, while physical activity was important with higher lymphocyte counts and populations of CD3+ cells (T cells), CD4+ cells (helper T cells), CD8+ cells (suppressor T cells), and CD20+ cells (B cells) in the more sedentary individuals.

In summary, these findings and the findings from past examinations do not provide evidence of a clinically meaningful dose-response effect for body burden of dioxin on parameters of immunologic assessment. The statistically significant relations emphasize the need for long-term evaluation.

17.4 SUMMARY

The immunologic assessment was based upon data gathered from laboratory collections. Associations with group (Model 1), initial dioxin (Model 2), categorized dioxin (Model 3), and 1987 dioxin levels (Model 4) were examined for each variable comprising the immunologic assessment.

17.4.1 Model 1: Group Analysis

Model 1 analyses revealed significant findings for both the unadjusted and adjusted analyses of CD16+56+ cell (natural killer cell) count and for the MSK smooth muscle antibody test. Each significant result was in the enlisted flyer occupational stratum. The mean CD16+56+ cell count was greater for Comparisons than for Ranch Hands, and a greater percentage of Comparisons had a smooth muscle antibody present than Ranch Hands. Marginally significant findings were found within the unadjusted examination of the CD16+56+ cell count when all occupations were combined, where the mean CD16+56+ cell count was greater for Comparisons than for Ranch Hands. This association was nonsignificant when adjusted for covariates. Among officers, a marginally significant difference in the percentage of the participants with the MSK mitochondrial antibody present was found in the adjusted analysis, where the antibody was more prevalent among Ranch Hands than among Comparisons. The CD3+ cell (T cell) count mean difference for enlisted groundcrew in the adjusted analysis was marginally significant. The CD3+ cell count mean was higher among Comparisons than Ranch Hands. Results for Model 1 analyses are summarized in Table 17-20.

Table 17-20. Summary of Group Analysis (Model 1) for Immunology Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED All	Officer	Enlisted Flyer	Enlisted Groundcrew
Laboratory				
CD3+ Cells (T Cells) (C)	ns	NS	ns	ns
CD4+ Cells (Helper T Cells) (C)	ns	NS	ns	ns
CD8+ Cells (Suppressor T Cells) (C)	ns	NS	ns	ns
CD16+56+ Cells (Natural Killer Cells) (C)	ns*	ns	−0.018	ns
CD20+ Cells (B Cells) (C)	ns	NS	ns	ns
CD3+CD4+ Cells (Helper T Cells) (C)	ns	NS	ns	ns
Absolute Lymphocytes (C)	ns	NS	ns	ns
IgA (C)	ns	ns	NS	ns
IgG (C)	ns	ns	ns	ns
IgM (C)	ns	ns	ns	ns
Lupus Panel: ANA Test (D)	NS	ns	NS	NS
Lupus Panel: ANA Thyroid Microsomal Antibody (D)	NS	NS	ns	NS
Lupus Panel: MSK Smooth Muscle Antibody (D)	NS	NS	−0.040	NS
Lupus Panel: MSK Mitochondrial Antibody (D)	NS	NS	ns	--
Lupus Panel: MSK Parietal Antibody (D)	NS	NS	ns	ns
Lupus Panel: Rheumatoid Factor (D)	ns	NS	NS	ns

Note: NS or ns: Not significant ($p>0.10$).
ns*: Marginally significant ($0.05<p\leq0.10$).
C: Continuous analysis.
D: Discrete analysis.
–: Relative risk<1.00 for discrete analysis; difference of means negative for continuous analysis.
--: Analysis not performed because of the sparse number of participants with the MSK mitochondrial antibody present.

P-value given if $p\leq0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Variable	ADJUSTED All	Officer	Enlisted Flyer	Enlisted Groundcrew
Laboratory				
CD3+ Cells (T Cells) (C)	ns	NS	ns	ns*
CD4+ Cells (Helper T Cells) (C)	ns	NS	ns	ns
CD8+ Cells (Suppressor T Cells) (C)	ns	NS	ns	ns
CD16+56+ Cells (Natural Killer Cells) (C)	ns	ns	−0.011	ns
CD20+ Cells (B Cells) (C)	ns	NS	ns	ns
CD3+CD4+ Cells (Helper T Cells) (C)	ns	NS	ns	ns
Absolute Lymphocytes (C)	ns	NS	ns	ns

Table 17-20. Summary of Group Analysis (Model 1) for Immunology Variables (Ranch Hands vs. Comparisons) (Continued)

Variable	ADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
IgA (C)	ns	ns	NS	ns
IgG (C)	ns	ns	ns	ns
IgM (C)	ns	ns	ns	ns
Lupus Panel: ANA Test (D)	NS	ns	NS	NS
Lupus Panel: ANA Thyroid Microsomal Antibody (D)	NS	NS	ns	NS
Lupus Panel: MSK Smooth Muscle Antibody (D)	ns	NS	–0.045	NS
Lupus Panel: MSK Mitochondrial Antibody (D)	NS	NS*	--	--
Lupus Panel: MSK Parietal Antibody (D)	NS	NS	ns	ns
Lupus Panel: Rheumatoid Factor (D)	ns	NS	ns	ns

Note: NS or ns: Not significant ($p>0.10$).
NS* or ns*: Marginally significant ($0.05<p\leq0.10$).
C: Continuous analysis.
D: Discrete analysis.
–: Relative risk<1.00 for discrete analysis; difference of means negative for continuous analysis.
--: Analysis not performed because of the sparse number of participants with the MSK mitochondrial antibody present.

P-value given if $p\leq0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

17.4.2 Model 2: Initial Dioxin Analysis

The Model 2 analyses revealed a significant association between CD20+ cell (B cell) count and initial dioxin for the unadjusted analysis and a marginally significant association for the adjusted analysis. The CD20+ cell count increased as initial dioxin increased. The association between initial dioxin and the CD3+CD4+ cell (helper T cells) count was marginally significant in the adjusted analysis, and the association between initial dioxin and IgA was significant in the adjusted analysis. The CD3+CD4+ cell count and IgA increased as initial dioxin increased. The association between initial dioxin and the MSK smooth muscle antibody test was marginally significant in both the unadjusted and adjusted analyses. The association between initial dioxin and the rheumatoid factor was significant in the unadjusted analysis. For both the MSK smooth muscle antibody and the rheumatoid factor, the percentage of Ranch Hands with a positive reading decreased as initial dioxin increased. Results for Model 2 analyses are summarized in Table 17-21.

Table 17-21. Summary of Initial Dioxin Analysis (Model 2) for Immunology Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Laboratory		
CD3+ Cells (T Cells) (C)	NS	NS
CD4+ Cells (Helper T Cells) (C)	NS	NS
CD8+ Cells (Suppressor T Cells) (C)	NS	NS
CD16+56+ (Natural Killer Cells) Cells (C)	ns	ns
CD20+ Cells (B Cells) (C)	+0.024	NS*
CD3+CD4+ Cells (Helper T Cells) (C)	NS	NS*
Absolute Lymphocytes (C)	NS	NS
IgA (C)	NS	+0.046
IgG (C)	ns	ns
IgM (C)	NS	ns
Lupus Panel: ANA Test (D)	NS	NS
Lupus Panel: ANA Thyroid Microsomal Antibody (D)	ns	ns
Lupus Panel: MSK Smooth Muscle Antibody (D)	ns*	ns*
Lupus Panel: MSK Mitochondrial Antibody (D)	−0.034	−0.049
Lupus Panel: MSK Parietal Antibody (D)	ns	ns
Lupus Panel: Rheumatoid Factor (D)	−0.033	ns

Note: NS or ns: Not significant ($p>0.10$).
NS* or ns*: Marginally significant ($0.05<p\leq0.10$).
C: Continuous analysis.
D: Discrete analysis.
+: Slope nonnegative for continuous analysis.
−: Relative risk<1.00 for discrete analysis.

P-value given if $p\leq0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or slope nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

17.4.3 Model 3: Categorized Dioxin Analysis

Results for Model 3 analyses are summarized in Table 17-22. The analysis found a significantly higher CD16+56+ cell (natural killer cell) count mean among Comparisons than Ranch Hands in the high dioxin category in both the unadjusted and adjusted analyses. A marginally significant smaller percentage of Ranch Hands in the high dioxin category had the MSK smooth muscle antibody present than did Comparisons in the unadjusted analysis. This difference between Ranch Hands and Comparisons was significant when adjusted for covariates. A significantly smaller percentage of Ranch Hands in the high dioxin category had a positive rheumatoid factor than did Comparisons in the unadjusted analysis. This difference between Ranch Hands and Comparisons was marginally significant when adjusted for covariates. A marginally significant difference in the presence of the MSK parietal antibody among Ranch Hands in the low dioxin category and Comparisons was found in the unadjusted analysis. The

percentage of participants with the parietal antibody present was higher among Ranch Hands in the low dioxin category than among Comparisons. After adjustment for covariates, the results were nonsignificant.

Table 17-22. Summary of Categorized Dioxin Analysis (Model 3) for Immunology Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Laboratory				
CD3+ Cells (T Cells) (C)	ns	ns	ns	ns
CD4+ Cells (Helper T Cells) (C)	ns	ns	NS	ns
CD8+ Cells (Suppressor T Cells) (C)	ns	ns	ns	ns
CD16+56+ Cells (Natural Killer Cells) (C)	ns	NS	–0.028	ns
CD20+ Cells (B Cells) (C)	ns	ns	NS	ns
CD3+CD4+ Cells (T Helper Cells) (C)	ns	ns	NS	ns
Absolute Lymphocytes (C)	NS	ns	NS	ns
IgA (C)	ns	ns	NS	NS
IgG (C)	ns	ns	ns	ns
IgM (C)	ns	ns	ns	ns
Lupus Panel: ANA Test (D)	NS	ns	NS	ns
Lupus Panel: ANA Thyroid Microsomal Antibody (D)	NS	NS	ns	ns
Lupus Panel: MSK Smooth Muscle Antibody (D)	NS	NS	ns*	ns
Lupus Panel: MSK Mitochondrial Antibody (D)	NS	NS	ns	NS
Lupus Panel: MSK Parietal Antibody (D)	ns	NS*	ns	NS
Lupus Panel: Rheumatoid Factor (D)	NS	NS	–0.032	ns

Note: NS or ns: Not significant (p>0.10).
NS* or ns*: Marginally significant (0.05<p≤0.10).
C: Continuous analysis.
D: Discrete analysis.
–: Relative risk<1.00 for discrete analysis; difference of means negative for continuous analysis.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 17-22. Summary of Categorized Dioxin Analysis (Model 3) for Immunology Variables (Ranch Hands vs. Comparisons) (Continued)

	ADJUSTED			
Variable	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Laboratory				
CD3+ Cells (T Cells) (C)	ns	ns	ns	ns
CD4+ Cells (Helper T Cells) (C)	ns	ns	ns	ns
CD8+ Cells (Suppressor T Cells) (C)	ns	ns	ns	ns
CD16+56+ Cells (Natural Killer Cells) (C)	ns	NS	−0.046	ns
CD20+ Cells (B Cells) (C)	NS	ns	ns	ns
CD3+CD4+ Cells (Helper T Cells) (C)	ns	ns	ns	ns
Absolute Lymphocytes (C)	NS	ns	ns	ns
IgA (C)	ns	ns	NS	NS
IgG (C)	ns	ns	ns	ns
IgM (C)	ns	ns	ns	ns
Lupus Panel: ANA Test (D)	NS	ns	NS	ns
Lupus Panel: ANA Thyroid Microsomal Antibody (D)	NS	NS	ns	ns
Lupus Panel: MSK Smooth Muscle Antibody (D)	NS	NS	−0.048	ns
Lupus Panel: MSK Mitochondrial Antibody (D)	NS	NS	--	--
Lupus Panel: MSK Parietal Antibody (D)	ns	NS	ns	NS
Lupus Panel: Rheumatoid Factor (D)	NS	NS	ns*	ns

Note: NS or ns: Not significant (p>0.10).
ns*: Marginally significant (0.05<p≤0.10).
C: Continuous analysis.
D: Discrete analysis.
–: Relative risk<1.00 for discrete analysis; difference of means negative for continuous analysis.
--: Analysis not performed because of the sparse number of participants with the MSK mitochondrial antibody present.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

17.4.4 Model 4: 1987 Dioxin Level Analysis

The Model 4 adjusted analyses uncovered significant associations between 1987 dioxin levels and CD3+ cell (T cell) count, CD4+ cell (helper T cell) count, and CD3+CD4+ cell (helper T cell) count. The cell counts increased as 1987 dioxin increased. Marginally significant associations with 1987 dioxin levels were found in the unadjusted analyses of IgA and MSK smooth muscle antibody. The IgA association showed an increase in IgA levels as 1987 dioxin increased. The percentage of Ranch Hands with a smooth muscle antibody present decreased as 1987 dioxin levels increased. The unadjusted analyses of the rheumatoid factor were significant, showing a decrease in the percentage of participants with a rheumatoid factor present as 1987 dioxin levels increased. All the significant or marginally significant

associations found in the unadjusted analyses were nonsignificant in the adjusted analyses. Results for Model 4 analyses are summarized in Table 17-23.

Table 17-23. Summary of 1987 Dioxin Analysis (Model 4) for Immunology Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Laboratory		
CD3+ Cells (T Cells) (C)	NS	+0.046
CD4+ Cells (Helper T Cells) (C)	NS	+0.033
CD8+ Cells (Suppressor T Cells) (C)	NS	NS
CD16+56+ Cells (Natural Killer Cells) (C)	NS	ns
CD20+ Cells (B Cells) (C)	NS	NS
CD3+CD4+ (Helper T Cells) Cells (C)	NS	+0.025
Absolute Lymphocytes (C)	NS	NS
IgA (C)	NS*	NS
IgG (C)	NS	ns
IgM (C)	ns	ns
Lupus Panel: ANA Test (D)	ns	ns
Lupus Panel: ANA Thyroid Microsomal Antibody (D)	ns	ns
Lupus Panel: MSK Smooth Muscle Antibody (D)	ns*	ns
Lupus Panel: MSK Mitochondrial Antibody (D)	ns	ns
Lupus Panel: MSK Parietal Antibody (D)	NS	NS
Lupus Panel: Rheumatoid Factor (D)	–0.010	ns

Note: NS or ns: Not significant ($p>0.10$).
NS* or ns*: Marginally significant ($0.05<p\leq0.10$).
C: Continuous analysis.
D: Discrete analysis.
+: Slope nonnegative for continuous analysis.
–: Relative risk<1.00 for discrete analysis.

P-value given if $p\leq0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or slope nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

17.5 CONCLUSION

The immunologic assessment was based upon laboratory data on six lymphocyte cell surface markers, absolute lymphocyte counts, three quantitative immunoglobulins, and six measurements from an autoantibody panel. The six cell marker measurements were carried out on a random sample of approximately 40 percent of the participants because of the complexity of the assay and the expense of the tests.

Group analyses revealed significant findings for the adjusted analyses of CD16+56+ cell (natural killer cell) count and for the MSK smooth muscle antibody test in enlisted flyers. Among enlisted flyers, the mean CD16+56+ cell count was greater for Comparisons than for Ranch Hands, and a greater percentage of Comparisons than Ranch Hands had a smooth muscle antibody present. For these analyses the

magnitude of the mean differences was small; therefore, the clinical importance of these findings is unknown.

Consistent with the previous two physical examinations, the mean serum concentration of IgA increased significantly with initial dioxin, but was not significantly increased in enlisted groundcrew or the high dioxin category; IgA did not increase significantly with 1987 dioxin. The IgA results, although significant, were small in magnitude and their clinical significance is unknown.

When comparing categorized dioxin levels between Ranch Hands and Comparisons, a significantly higher CD16+56+ cell count mean was observed among Comparisons than among Ranch Hands in the high dioxin category. Analyses revealed significant associations between 1987 dioxin levels and CD3+ cell (T cell) count, CD4+ cell (helper T cell) count, and CD3+CD4+ cell (helper T cell) count. The cell counts increased as 1987 dioxin increased.

In summary, these findings do not provide evidence of a biologically meaningful relation between body burden of dioxin and parameters of immunologic assessment. The statistically significant relations point out the need for long-term evaluation.

REFERENCES

1. Vos, J. G., J. A. Moore, and J. G. Zinkle. 1973. Effect of 2,3,7,8-tetrachlorodibenzo-p-dioxin on the immune system of laboratory animals. *Environmental Health Perspectives* 5:149-62.

2. Harris, M. W., J. A. Moore, J. G. Vos, and B. N. Gupta. 1972. General biological effects of TCDD in laboratory animals. *Environmental Health Perspectives* 5:101-9.

3. Kociba, R. J., P. A. Keeler, C. N. Park, and P. J. Gehring. 1976. 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD): Results of a 13-week oral toxicity study in rats. *Toxicology and Applied Pharmacology* 35:553-4.

4. Gupta, B. N., J. G. Vos, J. A. Moore, J. G. Zinkle, and B. C. Bullock. 1973. Pathologic effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin in laboratory animals. *Environmental Health Perspectives* 5:125-40.

5. Holsapple, M. P., N. K. Snyder, S. C. Wood, and D. L. Morris. 1991. A review of 2,3,7,8-tetrachlorodibenzo-p-dioxin-induced changes in immunocompetence: 1991 update. *Toxicology* 69:219-55.

6. Holsapple, M. P., S. L. Morris, S. C. Wood, and N. K. Snyder. 1991. 2,3,7,8-tetrachlorodibenzo-p-dioxin-induced changes in immunocompetence: Possible mechanisms. *Annual Review of Pharmacology and Toxicology* 31:73-100.

7. Vos, J. G., H. Van Loveren, and H. J. Schuurman. 1991. Immunotoxicity of dioxin: Immune function and host resistance in laboratory animals and humans. Banbury Report 35: Biological Basis for Risk Assessment of Dioxins and Related Compounds. Cold Spring Harbor Laboratory Press, pp. 79-93.

8. Schuurman, H. J., H. Van Loveren, J. Rozing, and J. Vos. 1992. Chemicals trophic for the thymus: Risk for immunodeficiency and autoimmunity. *International Journal of Immunopharmacology* 14:369-75.

9. Iverson, F., and D. L. Grant. 1991. Toxicology of the polychlorinated biphenyls, dibenzofurans and dibenzodioxins. *IARC Scientific Publications* 11:5-29.

10. Kerkvliet, N., and G. R. Burleson. 1994. Immunotoxicity of TCDD and related halogenated aromatic hydrocarbons. In: Dean, J. H., et al. (ed.), Target Organ Toxicology Series: Immunotoxicology and Immunopharmacology, Second Edition. Raven Press, New York: pp. 97-121.

11. Blaylock, B. L., S. D. Holladay, C. E. Comment, J. J. Heindel, and M. I. Luster. 1992. Exposure to tetrachlorodibenzo-p-dioxin (TCDD) alters fetal thymocyte maturation. *Toxicology and Applied Pharmacology* 112:207-13.

12. Holladay, S., P. Lindstrom, B. Blaylock, C. Comment, D. Germolec, J. Heindell, and M. Luster. 1991. Perinatal thymocyte antigen expression and postnatal immune development altered by gestational exposure to tetrachlorodibenzo-p-dioxin (TCDD). *Teratology* 44:385-93.

13. Luster, M. I., S. D. Holladay, B. L. Blaylock, D. R. Germolec, G. C. Clark, C. E. Comment, J. J. Heindel, and G. J. Rosenthal. 1992. TCDD inhibits murine thymocyte and B lymphocyte maturation. *Chemosphere* 25:115-8.

14. De Waal, E. J., L. H. P. M. Rademakers, H. J. Schuurman, H. Van Loveren, and J. G. Vox. 1993. Ultrastructure of the cortical epithelium of the rat thymus after in vivo exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Archives of Toxicology* 67:558-64.

15. Vos, J. G., and J. A. Moore. 1974. Suppression of cellular immunity in rats and mice by maternal treatment with 2,3,7,8-tetrachlorodibenzo-p-dioxin. *International Archives of Allergy* 47:777-94.

16. Faith, R. E., and J. A. Moore. 1977. Impairment of thymus-dependent immune functions by exposure of the developing immune system to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Journal of Toxicology and Environmental Health* 3:451-64.

17. Vecchi, A., A. Mantovani, M. Sironi, W. Luini, F. Spreafico, and S. Garattini. 1980. The effect of acute administration of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on humoral antibody production and cell-mediated activities in mice. *Archives of Toxicology Supplement* 4:163-5.

18. Clark, D. A., J. Gauldi, M. R. Szewczuk, and G. Sweeney. 1981. Enhanced suppressor cell activity as a mechanism of immunosuppression by 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Proceedings of the Society for Experimental Biology and Medicine* 168:290-9.

19. Thomas, P. T., and R. D. Hinsdill. 1979. The effect of perinatal exposure to tetrachlorodibenzo-p-dioxin on the immune response of young mice. *Drug and Chemical Toxicology* 2:77-98.

20. Holsapple, M. P., P. J. McNerney, D. W. Barnes, and K. L. White. 1984. Suppression of humoral antibody production by exposure to 1,2,3,6,7,8-hexachlorodibenzo-p-dioxin. *Journal of Pharmacology and Experimental Therapeutics* 231(3):518-26.

21. Kerkvliet, N. I., J. A. Brauner, and J. P. Matlock. 1985. Humoral immunotoxicity of polychlorinated diphenyl ethers, phenoxyphenols, dioxins and furans present as contaminants of technical grade pentachlorophenol. *Toxicology* 36:307-24.

22. Morris, D. L., N. K. Snyder, V. Gokani, R. E. Blair, and M. P. Holsapple. 1992. Enhanced suppression of humoral immunity in DBA/2 mice following subchronic exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Toxicology and Applied Pharmacology* 112:128-32.

23. Luster, M. I., G. A. Boorman, J. H. Dean, M. W. Harris, R. W. Luebke, M. L. Padarathsingh, and J. A. Moore. 1980. Examination of bone marrow, immunologic parameters and host susceptibility following pre- and postnatal exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *International Journal of Immunopharmacology* 2(4):301-10.

24. Luster, M. I., L. H. Hong, G. A. Boorman, G. Clark, H. T. Hayes, W. F. Greenlee, K. Dold, and A. N. Tucker. 1985. Acute myelotoxic responses in mice exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Toxicology and Applied Pharmacology* 81:156-65.

25. Chastain, J. E. Jr., and T. L. Pazdernik. 1985. 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)-induced immunotoxicity. *International Journal of Immunopharmacology* 7:849-56.

26. Fine, J. S., T. A. Gasiewicz, and A. E. Silverstone. 1989. Lymphocyte stem cell alterations following perinatal exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Molecular Pharmacology* 35:18-25.

27. Luster, M. I., D. R. Germolec, G. Clark, G. Wiegand, and G. J. Rosenthal. 1988. Selective effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and corticosteroid on in vitro lymphocyte maturation. *Journal of Immunology* 140:928-35.

28. White, K. L., and A. C. Anderson. 1985. Suppression of mouse complement activity by contaminants of technical grade pentachlorophenol. *Agents and Actions* 16(5):385-92.

29. White, K. L., H. H. Lysy, J. A. McCay, and A. C. Anderson. 1986. Modulation of serum complement levels following exposure to polychlorinated dibenzo-p-dioxins. *Toxicology and Applied Pharmacology* 84:209-19.

30. Lin, W. Q., and K. J. White. 1993. Production of complement component C3 in vivo following 2,3,7,8-tetrachlorodibenzo-p-dioxin exposure. *Journal of Toxicology and Environmental Health* 39:273-85.

31. Lin, W. Q., and K. J. White. 1993. Mouse Hepa 1c1c7 hepatoma cells produce complement component C3; 2,3,7,8-tetrachlorodibeno-p-dioxin fails to modulate this capacity. *Journal of Toxicology and Environmental Health* 39:27-41.

32. Thigpen, J. E., R. E. Faith, E. E. McConnell, and J. A. Moore. 1975. Increased susceptibility to bacterial infection as a sequela of exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Infection and Immunity* 12:1319-24.

33. Hinsdill, R. D., D. L. Couch, and R. S. Speirs. 1980. Immunosuppression in mice induced by dioxin (TCDD) in feed. *Journal of Environmental Pathology and Toxicology* 4:401-25.

34. Tucker, A. N., S. J. Vore, and M. I. Luster. 1986. Suppression of B cell differentiation by 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Molecular Pharmacology* 29:372-7.

35. House, R. V., L. D. Lauer, M. J. Murray, P. T. Thomas, J. P. Ehrlich, G. R. Burleson, and J. H. Dean. 1990. Examination of immune parameters and host resistance mechanisms in B6C3F1 mice following adult exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Journal of Toxicology and Environmental Health* 31:203-51.

36. Clark, D. A., G. Sweeney, S. Safe, E. Hancock, D. G. Kilburn, and J. Gauldie. 1983. Cellular and genetic basis for suppression of cytotoxic T cell generation by haloaromatic hydrocarbons. *Immunopharmacology* 6:143-53.

37. Poland, A., E. Glover, and A. S. Kende. 1976. Stereospecific high affinity binding of 2,3,7,8-tetrachlorodibenzo-p-dioxin by hepatic cytosols. Evidence that the binding species is a receptor for induction of aryl hydrocarbon hydroxylase. *Journal of Biological Chemistry* 251:4936-46.

38. Poland, A., and J. C. Knutson. 1982. 2,3,7,8-tetrachlorodibenzo-p-dioxin and related halogenated aromatic hydrocarbons: examination of the mechanism of toxicity. *Annual Review of Pharmacology and Toxicology* 22:517-54.

39. Okey, A. B., D. S. Riddick, and P. A. Harper. 1994. The Ah-receptor: Mediator of Toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and related compounds. *Toxicology Letters* 70:1-22.

40. Silbergeld, E. K., and T. A. Gasiewicz. 1989. Commentary: Dioxins and the Ah receptor. *American Journal of Industrial Medicine* 16:455-74.

41. Silkworth, J. B., and L. Antrim. 1986. Ah receptor mediated suppression of the antibody response in mice is dependent on the Ah genotype of lymphoid tissue. Abstract of a paper presented at the 25th Annual Meeting of the Society of Toxicology. *Toxicologist* 6:16.

42. Holsapple, M. P., N. K. Snyder, V. Gokani, R. E. Blair, and D. L. Morris. 1991. Role of Ah-receptor in suppression of in vivo antibody response by 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) is dependent on exposure conditions. *Federation of American Societies for Experimental Biology Journal* 5:A508.

43. Davis, D., and S. Safe. 1991. Halogenated aryl hydrocarbon-induced suppression of the in vitro plaque-forming cell response to sheep red blood cells is not dependent on the Ah receptor. *Immunopharmacology* 21:183-90.

44. Davis, D., and S. Safe. 1990. Immunosuppressive activities of polychlorinated biphenyls in C57B1/6N mice: structure-activity relationships as Ah receptor agonists and partial antagonists. *Toxicology* 63:97-111.

45. Vecchi, M., M. A. Sironi, M. A. Canegrati, M. Recchia, and S. Garattini. 1983. Immunosuppressive effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin in strains of mice with different susceptibility to induction of aryl hydrocarbon hydroxylase. *Toxicology and Applied Pharmacology* 68:434-41.

46. Kerkvliet, N. I., L. B. Steppan, J. A. Brauner, J. A. Deyo, M. C. Henderson, R. S. Tomar, and D. R. Buhler. 1990. Influence of the Ah locus on the humoral immunotoxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin: Evidence for Ah-receptor-dependent and Ah-receptor-independent mechanisms of immunosuppression. *Toxicology and Applied Pharmacology* 105:26-36.

47. Kerkvliet, N. I., L. Baecher-Steppan, B. B. Smith, J. A. Youngberg, M. C. Henderson, and D. R. Buhler. 1990. Role of the Ah locus in suppression of cytotoxic T lymphocyte activity by halogenated aromatic hydrocarbons (PCBs and TCDD): Structure-activity relationships and effects in C57BL/6 mice congenic at the Ah locus. *Fundamentals of Applied Toxicology* 14:532-41.

48. Pavlyak, A. L., S. M. Wielgosz, and E. Huttner. 1989. Proliferation of splenic lymphocytes is inhibited more strongly by 2,3,7,8-tetrachlorodibenzo-p-dioxin in C57BL/10 (Ah+Ah+) mice than in DBA/2 (Ah-Ah-) mice. *Bulletin for Experimental Biology and Medicine* 107:365-6.

49. Lysy, H. H., J. A. McCay, and K. L. White. 1986. A structure activity relationship of dioxin suppression of complement activity and segregation with the Ah locus. Abstract of a paper presented at the 25th Annual Meeting of the Society of Toxicology. *Toxicologist* 6:171.

50. Dooley, R. K., and M. P. Holsapple. 1987. The primary cellular target responsible for tetrachlorodibenzo-p-dioxin (TCDD)-induced immunosuppression is the B-lymphocyte. *Federal Proceedings* 46:541.

51. Kramer, C. M., K. W. Johnson, R. K. Dooley, and M. P. Holsapple. 1987. 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) enhances antibody production and protein kinase activity in murine B cells. *Biochemical and Biophysical Research Communications* 145:25-33.

52. Neubert, R., U. Jacob-Muller, R. Stahlmann, H. Helge, and D. Neubert. 1990. Polyhalogenated dibenzo-p-dioxins and dibenzofurans and the immune system: 1. Effects on peripheral lymphocyte subpopulations of a non-human primate (Callithrix jacchus) after treatment with 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Archives of Toxicology* 64:345-59.

53. Neubert, R., U. Jacob-Muller, H. Helge, R. Stahlmann, and D. Neubert. 1991. Polyhalogenated dibenzo-p-dioxins and dibenzofurans and the immune system: 2. In vitro effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on lymphocytes of venous blood from man and a nonhuman primate (Callithrix jacchus). *Archives of Toxicology* 65:213-9.

54. Neubert, R., G. Golor, R. Stahlmann, H. Helge, and D. Neubert. 1992. Polyhalogenated dibenzo-p-dioxins and dibenzofurans and the immune system: 4. Effects of multiple dose treatment with 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on peripheral lymphocyte subpopulations of a nonhuman primate (Callithrix jacchus). *Archives of Toxicology* 66:250-9.

55. Neubert, R., G. Golor, R. Stahlmann, H. Helge, and D. Neubert. 1992. Dose-dependent TCDD-induced increase or decrease in T-lymphocyte subsets in the blood of New World monkeys (Callithrix jacchus). *Chemosphere* 25:1201-6.

56. Neubert, R., H. Helge, and D. Neubert. 1994. Proliferative capacity of marmoset lymphocytes after tetanus vaccination and lack of 2,3,7,8-tetrachlorodibenzo-p-dioxin to reduce a booster effect. *Life Sciences* 56:437-44.

57. Hong, R. 1991. Effects of environmental toxins on lymphocyte function: studies in rhesus and man. *Annals of Allergy* 66:474-80.

58. Lorenzen, A., and A. B. Okey. 1991. Detection and characterization of Ah receptor in tissue and cells from human tonsils. *Toxicology and Applied Pharmacology* 107:203-14.

59. Wood, S. C., H. G. Jeong, D. L. Morris, and M. P. Holsapple. 1993. Direct effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on human tonsillar lymphocytes. *Toxicology* 81:131-43.

60. Wood, S. C., and M. P. Holsapple. 1993. Direct suppression of superantigen-induced IgM secretion in human lymphocytes by 2,3,7,8-TCDD. *Toxicology and Applied Pharmacology* 122:308-13.

61. Mehta, S., A. Holm, T. Mezzanotti, and R. Kurl. 1992. Effect of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on human lymphocyte maturation. *Chemosphere* 25:1095-100.

62. Neubert, R., L. Maskow, J. Webb, U. Jacob-Muller, A. C. Nogueira, I. Delgado, H. Helge, and D. Neubert. 1993. Chlorinated dibenzo-p-dioxins and dibenzofurans and the human immune system: 1. Blood cell receptors in volunteers with moderately increased body burdens. *Life Sciences* 53:1995-2006.

63. Neubert, R., L. Maskow, I. Delgado, H. Helge, and D. Neubert. 1994. Chlorinated dibenzo-p-dioxins and dibenzofurans and the human immune system: 2. In vitro proliferation of lymphocytes from workers with quantified moderately increased body burdens. *Life Sciences* 56:421-36.

64. Pocchiari, F., V. Silano, and A. Zampieri. 1979. Human health effects from accidental release of tetrachlorodibenzo-p-dioxin (TCDD) at Seveso, Italy. *Annals of the New York Academy of Sciences* 320:311-20.

65. Reggiani, G. 1978. Medical problems raised by the TCDD contamination in Seveso, Italy. *Archives of Toxicology* 40:161-88.

66. Ghezzi, I., P. Cannatelli, G. Assennato, F. Merlo, P. Mocarelli, P. Brambilla, and F. Sicurello. 1982. Potential 2,3,7,8-tetrachlorodibenzo-p-dioxin exposure of Seveso decontamination workers. A controlled prospective study. *Scandinavian Journal of Work, Environment, and Health* 8:176-9.

67. Sirchia, G. G. 1980. Exposure to TCDD: immunologic effects. In: NRC Workshop: plans for clinical and epidemiologic follow-up after area-wide chemical contamination. Washington, DC: National Academy Press 234-66.

68. Tognoni, G., and A. Bonaccorsi. 1982. Epidemiological problems with TCDD (a critical view). *Drug Metabolism Reviews* 13:447-69.

69. Mocarelli, P., A. Marocchi, P. Brambilla, P. Gerthoux, C. Beretta, L. Colombo, M. Bertona, C. Sarto, P. Tramacere, A. Mondonico, C. Crespi, S. Signorini, and R. Brivio. 1992. Human data derived from the Seveso accident: relevance for human risk assessment. *Toxic Substances Journal* 12:151-73.

70. Mocarelli, P., A. Marocchi, P. Brambilla, P. Gerthoux, L. Colombo, A. Mondonico, and L. Meazza. 1991. Effects of dioxin exposure in humans at Seveso, Italy. Branbury Report 35 (Biological Basis for Risk Assessment of Dioxins and Related Compounds):95-110.

71. Jennings, A. M., G. Wild, J. D. Ward, and A. M. Ward. 1988. Immunological abnormalities 17 years after accidental exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *British Journal of Industrial Medicine* 45:701-4.

72. May, G. 1982. Tetrachlorodibenzodioxin: A survey of subject ten years after exposure. *British Journal of Industrial Medicine* 39:128-35.

73. Jansing, P. J., and R. Korff. 1994. Blood levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin and gamma-globulins in a follow-up investigation of employees with chloracne. *Journal of Dermatological Science* 8:91-5.

74. Ott, M. G., A. Zober, and C. Germann. 1994. Laboratory results for selected target organs in 128 individuals occupationally exposed to TCDD. *Chemosphere* 29:2423-37.

75. Von Benner, A., L. Edler, K. Mayer, and A. Zober. 1994. 'Dioxin' investigation program of the chemical industry professional association. *Arbeitsmedizin Sozialmedizin Praventivmedizin* 29:11-6.

76. Knutsen, A. P. 1984. Immunologic effects of TCDD exposure in humans. *Bulletin of Environmental Contamination and Toxicology* 33:673-81.

77. Hoffman, R. E., P. A. Stehr-Stahl, K. B. White, G. Evans, A. P. Knutsen, W. F. Schramm, J. L. Staake, B. B. Gibson, and K. K. Steinberg. 1986. Health effects of long-term exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Journal of the American Medical Association* 255:2031-8.

78. Knutsen, A. P., S. T. Roodman, R. G. Evans, K. R. Mueller, K. B. Webb, P. Stehr-Green, R. E. Hoffman, and W. F. Schramm. 1987. Immune studies in TCDD-exposed Missouri residents: Quail Run. *Bulletin of Environmental Contamination and Toxicology* 39:481-9.

79. Evans, R. G., K. B. Webb, A. P. Knutsen, S. T. Roodman, D. W. Roberts, J. R. Bagby, W. A. Garret, and J. S. Andrews. 1988. A medical follow-up of the health effects of long term exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Archives of Environmental Health* 43:273-8.

80. Webb, K., R. G. Evans, P. Stehr, and S. M. Ayres. 1987. Pilot study on health effects of environmental 2,3,7,8-TCDD in Missouri. *American Journal of Industrial Medicine* 11:685-91.

81. Webb, K. B., R. G. Evans, A. P. Knutsen, S. T. Roodman, D. W. Roberts, W. F. Schramm, B. B. Gibson, J. S. Andrews Jr., L. L. Needham, and D. G. Patterson. 1989. Medical evaluation of subjects with known body levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Journal of Toxicology and Environmental Health* 28:183-93.

82. Lathrop, G. D., W. H. Wolfe, R. A. Albanese, and P. M. Moynahan. 1984. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Baseline Morbidity Study Results. NTIS: AD A-138-340. United States Air Force School of Aerospace Medicine, Brooks Air Force Base, Texas.

83. Lathrop, G. D., S. G. Machado, T. G. Karrison, W. D. Grubbs, W. F. Thomas, W. H. Wolfe, J. E. Michalek, J. C. Miner, and M. R. Peterson. 1987. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: First followup examination results. NTIS: AD A 188262. United States Air Force School of Aerospace Medicine, Brooks Air Force Base, Texas.

84. Thomas, W. F., W. D. Grubbs, T. G. Karrison, M. B. Lustik, R. H. Roegner, D. E. Williams, W. H. Wolfe, J. E. Michalek, J. C. Miner, and R. W. Ogershok. 1990. An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: I. 1987 followup examination results, May 1987 to January 1990. NTIS: AD A 222 573. United States Air Force School of Aerospace Medicine, Human Systems Division (AFSC), Brooks Air Force Base, Texas.

85. Roegner, R. H., W. D. Grubbs, M. B. Lustik, A. S. Brockman, S. C. Henderson, D. E. Williams, W. H. Wolfe, J. E. Michalek, and J. C. Miner. 1991. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides. Serum dioxin analysis of 1987 examination results. NTIS: AD A 237 516-24. United States Air Force School of Aerospace Medicine, Brooks Air Force Base, Texas.

86. Grubbs, W. D., W. H. Wolfe, J. E. Michalek, D. E. Williams, M. B. Lustik, A. S. Brockman, S. C. Henderson, F. R. Burnett, R. G. Land, D. J. Osborne, V. K. Rocconi, M. E. Schreiber, J. C. Miner, G. L. Henriksen, and J. A. Swaby. 1995. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final Report. 1992 Followup Examination Results. NTIS: AD A 304 306, 304 308-316. United States Air Force School of Aerospace Medicine, Brooks Air Force Base, Texas.

87. Moran, R. A., C. W. Lee, J. M. Fujimoto, and N. J. Calvanico. 1986. Effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on IgA serum and bile levels in rats. *Immunopharmacology* 12:245-50.

88. Piani, A., and C. Schoenborn. 1990. Health promotion and disease prevention: United States. National Center for Health Statistics. Vital Health Statistics 10.

89. Stephens, T., and C. L. Craig. 1989. Fitness and Activity Measurement in the 1981 Canada Fitness Survey. Assessing Physical Fitness and Physical Activity in Population-Based Surveys. National Center for Health Statistics. Thomas F. Drury, ed. DHHS Pub. No. (PHS) 89-1253. Public Health Service. Washington, DC. U.S. Government Printing Office.

90. Michalek, J. E., J. L. Pirkle, S. P. Caudill, R. C. Tripathi, D. G. Patterson Jr., and L. L. Needham. 1996. Pharmacokinetics of TCDD in Veterans of Operation Ranch Hand: 10-year Followup. *Journal of Toxicology and Environmental Health* 47:209-20.

Table of Contents

List of Tables

18 PULMONARY ASSESSMENT

18.1 INTRODUCTION

18.1.1 Background

Apart from irritative tracheo-bronchial symptoms occurring consequent to industrial accidents, there is no evidence that the human lung is a target organ for 2,3,7,8-tetrachlorodibenzo-p-dioxin (dioxin) toxicity. A single case of hypersensitivity pneumonitis was described in a Vietnam veteran occupationally exposed to herbicides (1). The respiratory failure that has been reported in rare cases of extreme phenoxy herbicide intoxication appears to be related to central nervous system depression rather than primary pneumotoxicity (2, 3).

Research into the pulmonary toxicity of dioxin in laboratory animals has focused on the physicochemical properties of the cytosolic aryl hydrocarbon (Ah) receptor and the carcinogenic potential of the cytochrome P-450 enzyme system in mice (4), rats (5, 6), and rabbits (7–12). Although these studies have demonstrated that dioxin enhances the activity of cytochrome P-450 and of aryl hydrocarbon hydroxylase in respiratory tract epithelium, the relevance to the development of lung disease in humans is uncertain.

Other lines of research have heightened interest in the possibility that dioxin might cause pneumotoxicity in humans. In one study (13), cytosol preparations were examined from human lung tissue specimens obtained at surgery. Only 10 of 53 specimens had detectable Ah receptors that were present at concentrations far less (10 to 30 percent) than those found in lung cytosols from laboratory animals. In mice, the induction of cytochrome P-450 enzymes by dioxin in lung was found similar to that in liver (14). In rats (15, 16), the intratracheal administration of dioxin was associated with significant dose-related increases in hepatic enzymes as well, establishing the transpulmonary absorption of dioxin and the potential for pneumotoxicity.

Lung disease has been included infrequently as a clinical endpoint in epidemiological studies of humans exposed to phenoxy herbicides. In one report (17), standard pulmonary function tests were included in clinical examinations of 367 employees 30 years after a chemical industrial explosion associated with high level exposure to 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) and, by contamination, to dioxin. Although tissue levels of dioxin were not available, 55 percent of the exposed cohorts developed chloracne, reflecting the severity of exposure. The prevalence of abnormal chest radiographs was similar in the exposed and unexposed cohorts. Significant reductions in dynamic indices of lung function were limited to cigarette smokers. In this sub-cohort, a significant reduction in forced expiratory volume at one second (FEV_1) was noted, as was a reduction in forced vital capacity (FVC). Even after adjustment for cumulative cigarette use, the predicted means for FEV_1, FVC, and the derived index, FEV_1/FVC, were significantly reduced in the exposed cohort relative to controls. These results raise the possibility that cigarette use may sensitize the lungs and make them more vulnerable as a target organ for dioxin toxicity.

In a more recent occupational morbidity study conducted by the National Institute of Occupational Safety and Health (NIOSH) (18)—one of the first to include tissue levels of dioxin in the analyses—the prevalence of two chronic pulmonary diseases, emphysema and chronic bronchitis, was determined in 281 workers exposed to dioxin for 15 years in two chemical production factories and compared with 260 unexposed controls. The clinical examination protocol was similar to the one used in the current Air Force Health Study (AFHS) and included dynamic indices of lung function (FEV_1, FVC, and FEV_1/FVC)

and, on the physical examination, nine abnormalities of the thorax and lungs. These nine abnormalities were asymmetric chest excursion, abnormal chest shape, abnormal chest expansion, hyperresonant lungs, dullness to percussion, diminished breath sounds, crackles on auscultation, wheezes on auscultation, and pleural friction rub. The body burden of dioxin was determined by serum dioxin levels: mean level of 220 parts per trillion (ppt) in the exposed cohort versus 7 ppt in the controls. In contrast to the results cited above, the incidence of chronic lung disease and the prevalence of abnormal physical findings and pulmonary function tests were similar in the exposed and control groups.

Although several animal experiments have documented the occurrence of lung cancers associated with dioxin toxicity in rats (19, 20), mice (21), and monkeys (22), numerous large-scale epidemiological studies in humans exposed occupationally (23, 24), as a consequence of industrial accidents (25–27) or during military service (28–35), found no increase in the occurrence of lung cancer in populations at risk. In another large retrospective occupational study conducted by NIOSH, mortality associated with cancers of the respiratory tract was significantly increased, but only in a sub-cohort of workers with more than one year exposure and greater than 20 years of latency (36).

In one report, Marine veterans who served in Vietnam were found to be at increased risk for the development of lung cancer (37). A subsequent proportionate mortality study conducted by the Veterans' Administration reviewed the data and concluded that the apparent increase in risk might have been related to a lower than expected mortality from lung cancer in the control group of Marines who did not serve in Vietnam (38).

In the 1987 AFHS examinations, Ranch Hand participants were more likely than Comparisons to have abnormalities of the thorax and lungs (39). This finding also was seen in the 1992 examination (40). Differences between Ranch Hands and Comparisons were not seen in the laboratory measurements in 1987 or 1992. In both examinations, a slight reduction in FVC and, as a consequence, an increase in the FEV_1 to FVC ratio were noted in association with increasing serum dioxin levels. Although consistent with a subtle dose-response effect, the differences in the means were too small to be physiologically meaningful.

18.1.2 Summary of Previous Analyses of the Air Force Health Study

18.1.2.1 1982 Baseline Study Summary Results

The 1982 baseline examination explored historical pulmonary disease by questionnaire and active pulmonary function by standardized spirometric technique. These areas were of significant interest because of reported operational inhalation of Herbicide Orange by some Ranch Hand enlisted flyers and enlisted groundcrew.

The questionnaire revealed no group differences for historical diagnoses of tuberculosis and fungal infections, pneumonia, cancer, or chronic sinusitis and upper respiratory disease. At the physical examination, the Ranch Hand and Comparison unadjusted means for FEV_1 (percent predicted), FVC, and the ratio of FEV_1 to FVC were similar. Adjusted mean values were not calculated because of significant interactions (group-by-age for FEV_1 and FVC, group-by-smoking for the ratio of FEV_1 to FVC).

Exposure analyses showed two significant associations in the enlisted flyer and enlisted groundcrew strata, but neither was indicative of a linear dose-response. Attempts to adjust the means of the pulmonary function values for age and smoking revealed several interactions, but the results were essentially negative. Overall, there were no pulmonary diseases, pulmonary function data, or associations of concern.

18.1.2.2 1985 Follow-up Study Summary Results

Because of the lack of significant results from the pulmonary analyses from the baseline examination, pulmonary function (spirometric) studies were not performed during the 1985 follow-up examination. Collection of pulmonary data was limited to a questionnaire history of respiratory disease, physical examination of the thorax and lungs, and pulmonary abnormalities detected on a routine chest x ray. Mortality because of respiratory disease also was evaluated.

There were no significant group differences found for reported history of asthma, bronchitis, pleurisy, or tuberculosis based on the unadjusted analyses. Adjustments for age and lifetime smoking did not alter the findings of group similarity, although there was a significant group-by-lifetime smoking interaction for pleurisy and tuberculosis. Ranch Hands who were moderate lifetime smokers (up to 10 pack-years) had a significantly increased incidence of pleurisy and tuberculosis than did Comparisons who were moderate lifetime smokers.

Similarly, there were no significant group differences in the unadjusted analyses for the radiological and clinical respiratory findings of thorax and lungs, asymmetrical expansion, hyperresonance, dullness, wheezes, rales, and x-ray interpretations. These findings were supported by the adjusted analyses. Also, the exposure index analyses revealed no consistent dose-response pattern.

18.1.2.3 1987 Follow-up Study Summary Results

The pulmonary assessment was based on five self-reported respiratory illnesses, seven clinical observations, and eight laboratory measurements. The self-reported illnesses were based on participant-reported responses to the personal history form and the health history questionnaire. No evidence of an herbicide effect was detected in the assessment of the reported respiratory illnesses. The health of the two groups was comparable based on the clinical and laboratory variables, although Ranch Hands had a significantly higher percentage of thorax and lung abnormalities on examination than did Comparisons, based on the unadjusted analysis, and a marginally higher percentage after adjustment for covariates. No significant group differences were detected in the adjusted analyses when comparing all Ranch Hands with all Comparisons. Exploration of interactions did not reveal a consistent pattern indicating an herbicide effect. The adverse effects of smoking on pulmonary status were evident in all analyses.

18.1.2.4 Serum Dioxin Analysis of 1987 Follow-up Study Summary Results

In general, there was no association between initial dioxin levels and the discrete variables. For the continuous variables, there appeared to be a negative association with initial dioxin. The associations with current dioxin did not differ significantly between the two time strata for any of the variables. In the categorized current dioxin analyses, the percentage of abnormalities did not differ significantly among the four current dioxin categories for any of the questionnaire and physical examination variables, except under the adjusted analysis of thorax and lung abnormalities. In this case, Ranch Hands in the low and high categories had a higher percentage of abnormalities than did Comparisons in the background category; but Ranch Hands in the unknown category had a lower percentage of abnormalities than did Comparisons in the background category. For the continuous variables, the means differed among the current dioxin categories. For FVC, FEV_1, and forced expiratory flow maximum (FEFmax), the mean for the Ranch Hands in the unknown category tended to be greater than the mean for the Comparisons in the background category, but the means for the low and high categories were less than the mean for the background category. In the analysis of the ratio of observed FEV_1 to observed FVC, this trend was reversed.

In the longitudinal analysis of the ratio of observed FEV_1 to observed FVC, there was a significant positive association with current dioxin and a significant difference among the current dioxin categories,

with the mean increase from 1982 to 1987 in the high category greater than the mean increase from 1982 to 1987 in the background category.

In summary, the historical, physical examination, and laboratory data analyzed in the 1987 serum dioxin follow-up study revealed no evidence for an increased occurrence of pulmonary disease in the Ranch Hand cohort in relation to the body burden of dioxin. Analysis of two laboratory variables, FVC and the ratio of observed FEV_1 to observed FVC, yielded results that were consistent with subtle dose-response effects related to the body burden of dioxin in Ranch Hands. Body habitus and, more specifically, body fat might have played a role in these associations between dioxin and pulmonary function indices.

18.1.2.5 1992 Follow-up Study Summary Results

For the medical records and physical examination pulmonary variables, the group analysis revealed significant relations for bronchitis and thorax and lung abnormalities only. For enlisted flyers, significantly more Ranch Hands than Comparisons had bronchitis and thorax and lung abnormalities. The initial dioxin, categorized dioxin, and current dioxin analyses for these variables did not confirm a dioxin dose-response relation.

For the laboratory variables, a statistically significant inverse relation was revealed between percent of predicted FVC and initial and current dioxin for Ranch Hands. When Ranch Hands were contrasted with Comparisons, no significant differences were detected. Also, the analysis of the ratio of observed FEV_1 to observed FVC within Ranch Hands revealed a significant direct relation with initial dioxin indicating that the ratio increases (becomes closer to 1) for increasing levels of initial dioxin, which may have been due to the diminishing magnitude of FVC in the denominator of the ratio.

In the longitudinal analysis of the ratio of observed FEV_1 to observed FVC, there was a significant group difference for the enlisted flyers. The Ranch Hand enlisted flyers had a larger decrease in the ratio between 1982 and 1992 than did the Comparison enlisted flyers.

In summary, the historical, physical examination, and laboratory data analyzed for this assessment revealed no consistent evidence of an increased prevalence of pulmonary disease in the Ranch Hand cohort in relation to body burden of dioxin.

18.1.3 Parameters for the 1997 Pulmonary Assessment

18.1.3.1 Dependent Variables

The pulmonary assessment was based on questionnaire, physical examination, and laboratory data collected at the 1997 follow-up examination.

18.1.3.1.1 Medical Records Data

In the self-administered family and personal history section, each study participant was asked whether he had ever experienced asthma, bronchitis, or pneumonia. The following International Classification of Diseases, 9^{th} Revision, Clinical Modification (ICD-9-CM) codes were used: asthma: 493.0–493.9; bronchitis: 466.0–466.1, 490, 491.0–491.9, 494; and pneumonia: 480.0–486, 487.0. This self-reported information was combined with information from the 1997 physical examination; the 1985, 1987, and 1992 follow-up questionnaires and physical examinations; and the baseline questionnaire and examination and, subsequently, was verified by a review of the participant's medical records. These three variables were individually analyzed as measures of the pulmonary health status of each participant.

Participants with occurrences of asthma, bronchitis, or pneumonia before duty in Southeast Asia (SEA) were excluded from the analyses of the respective variables.

18.1.3.1.2 Physical Examination Data

Part of the pulmonary assessment was based on the results of the physical examination of the thorax and lungs. A composite variable, thorax and lung abnormalities, was constructed based on the presence or absence of asymmetrical expansion, hyperresonance, dullness, wheezes, rales, or chronic obstructive pulmonary disease, as well as the physician's assessment of abnormality. This variable was coded as "abnormal" if any of these conditions was present and "normal" if none of these conditions was present. No participants were excluded for medical reasons from the analysis of this variable.

18.1.3.1.3 Laboratory Examination Data

The assessment of the laboratory examination data included the analysis of pulmonary abnormalities detected on a routine chest x ray. This variable was coded as "normal" or "abnormal." The assessment also included the analysis of pulmonary physiologic data collected during the physical examination employing standard spirometric techniques. Numerous indices were derived, including FVC—a measurement of the amount of air in liters expelled from maximum inspiration to full expiration—and FEV_1 in liters, an index derived from the FVC that quantifies the amount of air expelled at 1 second. The values used for these variables were the percentages of predicted values rather than the actual volume or flow rate. The calculations of these percentages included an adjustment for age and height, as prescribed by the American Thoracic Society. The laboratory used the same predictive values regardless of race. For these indices, lower values indicated greater compromise in the lung function. In addition, the ratio of observed FEV_1 to observed FVC was calculated as an index reflective of obstructive airway disease. These variables were analyzed as continuous variables.

Loss of vital capacity and obstructive abnormality were classified by the examiner as none, mild, moderate, or severe and were analyzed as part of the pulmonary assessment. Results judged to be between none and mild were classified as "mild" for all analyses. A similar methodology was used for results between mild and moderate (i.e., classified as "moderate") and between moderate and severe (i.e., classified as "severe"). Because of the low frequencies in the moderate and severe categories, these two categories were combined in the analysis of loss of vital capacity. No participants were excluded for medical reasons from the analysis of these variables.

As a guideline for categorizing loss of vital capacity and obstructive abnormality, the following percent reductions in the FVC and FEV_1/FVC, respectively, were used:

- Mild: 70–100%
- Moderate: 60–69%
- Moderately severe: 50–59%
- Severe: 34–49%
- Very severe: <34%.

These categorizations are based on American Thoracic Society criteria (41). The percent reductions in the FVC and the FEV_1/FVC were based on the percent of predicted values, which were adjusted for age and height.

18.1.3.2 Covariates

The effects of age, race, military occupation, current cigarette smoking (cigarettes/day), lifetime cigarette smoking history (pack-years), body fat (percent), and exposure to industrial chemicals (yes, no) were used in adjusted statistical analyses evaluating the pulmonary dependent variables. Current cigarette smoking was used as a covariate for the physical examination and laboratory variables only. The current level of cigarette smoking was not appropriate as a risk factor for an endpoint based on post-SEA history. Lifetime cigarette smoking history was used to investigate the cumulative effects of cigarette smoking on these endpoints.

Age, race, and occupation were determined from military records. Current cigarette smoking and lifetime cigarette smoking history were based on questionnaire data. For lifetime cigarette smoking history, the respondent's average smoking was estimated over his lifetime based on his responses to the 1997 questionnaire, with 1 pack-year defined as 365 packs of cigarettes smoked during a single year. The participant's lifetime exposure through 1992 to industrial chemicals was updated with information reported in the 1997 questionnaire.

Body fat was calculated from a metric body mass index (42); the formula is

$$Body\ Fat\,(in\ percent) = \frac{Weight\,(kg)}{[Height\,(m)]^2} \bullet 1.264 - 13.305.$$

For purposes of covariate associations for discrete dependent variables, body fat was dichotomized as "lean or normal" (≤25 percent) and "obese" (>25 percent).

18.1.4 Statistical Methods

Table 18-1 summarizes the statistical analyses performed for the pulmonary assessment. The first part of this table lists the dependent variables analyzed, source of the data, form of the data, cutpoints, covariates, and statistical methods. The second part of the table further describes the covariates. A covariate was used in its continuous form whenever possible for all adjusted analyses; if the covariate was inherently discrete (e.g., military occupation), or if a categorized form was needed to develop measures of association with the dependent variables, the covariate was categorized as shown in Table 18-1. Table 18-2 provides a summary of participants with missing dependent variable and covariate data. In addition, the number of participants excluded because of pre-SEA conditions is given.

Table 18-1. Statistical Analysis for the Pulmonary Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
Asthma	MR-V	D	Yes No	(1)	(a)	U:LR A:LR
Bronchitis	MR-V	D	Yes No	(1)	(a)	U:LR A:LR
Pneumonia	MR-V	D	Yes No	(1)	(a)	U:LR A:LR

Table 18-1. Statistical Analysis for the Pulmonary Assessment (Continued)

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
Thorax and Lung Abnormalities	PE	D	Yes No	(2)	None	U:LR A:LR
X-ray Interpretation	LAB	D	Abnormal Normal	(2)	None	U:LR A:LR
Forced Vital Capacity (FVC) (percent of predicted)	LAB	C	--	(2)	None	U:GLM A:GLM
Forced Expiratory Volume in 1 Second (FEV_1) (percent of predicted)	LAB	C	--	(2)	None	U:GLM A:GLM
Ratio of Observed FEV_1 to Observed FVC	LAB	C	--	(2)	None	U:GLM A:GLM L:GLM
Loss of Vital Capacity	LAB	D	Moderate/Severe Mild None	(2)	None	U:PR A:PR
Obstructive Abnormality	LAB	D	Severe Moderate Mild None	(2)	None	U:PR A:PR

[a]Covariates:
(1): age, race, military occupation, lifetime cigarette smoking history, body fat, exposure to industrial chemicals.
(2): age, race, military occupation, current cigarette smoking, lifetime cigarette smoking history, body fat, exposure to industrial chemicals.

[b]Exclusions:
(a): participants with a pre-SEA history of the disorder.

Covariates

Variable (Units)	Data Source	Data Form	Cutpoints
Age (years)	MIL	D/C	Born≥1942 Born<1942
Race	MIL	D	Black Non-Black
Occupation	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Current Cigarette Smoking (cigarettes/day)	Q-SR	D/C	0-Never 0-Former >0–20 >20
Lifetime Cigarette Smoking History (pack-years)	Q-SR	D/C	0 >0–10 >10

Table 18-1. Statistical Analysis for the Pulmonary Assessment (Continued)

Variable (Units)	Data Source	Data Form	Cutpoints
Body Fat (percent)	PE	D/C	Lean or Normal: ≤25% Obese: >25%
Industrial Chemicals Exposure	Q-SR	D	Yes No

Abbreviations

Data Source: LAB: 1997 laboratory results
MIL: Air Force military records
MR-V: Medical records (verified)
PE: 1997 physical examination
Q-SR: Health questionnaires (self-reported)

Data Form: C: Continuous analysis only
D: Discrete analysis only
D/C: Appropriate form for analysis (either discrete or continuous)

Statistical Analysis: U: Unadjusted analysis
A: Adjusted analysis
L: Longitudinal analysis

Statistical Methods: GLM: General linear models analysis
LR: Logistic regression analysis
PR: Polytomous logistic regression analysis

Table 18-2. Number of Participants Excluded or with Missing Data for the Pulmonary Assessment

		Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
Variable	Variable Use	Ranch Hand	Comparison	Initial	1987	Ranch Hand	Comparison
X-ray Interpretation	DEP	2	0	2	2	2	0
FVC	DEP	1	2	1	1	1	2
FEV_1	DEP	1	2	1	1	1	2
Ratio of the Observed FEV_1 to Observed FVC	DEP	1	2	1	1	1	2
Loss of Vital Capacity	DEP	1	2	1	1	1	2
Obstructive Abnormality	DEP	1	2	1	1	1	2
Current Cigarette Smoking	COV	1	0	0	1	1	0
Lifetime Cigarette Smoking History	COV	2	1	1	2	2	1
Pre-SEA Asthma	EXC	11	5	7	11	11	5
Pre-SEA Bronchitis	EXC	24	27	15	24	24	25
Pre-SEA Pneumonia	EXC	44	47	24	44	44	45

Table 18-2. Number of Participants Excluded or with Missing Data for Pulmonary Assessment (Continued)

Note: DEP = Dependent variable.
COV = Covariate.
EXC = Exclusion.
870 Ranch Hands and 1,251 Comparisons.
482 Ranch Hands for initial dioxin; 863 Ranch Hands for 1987 dioxin.
863 Ranch Hands and 1,213 Comparisons for categorized dioxin.

18.1.4.1 Longitudinal Analysis

Longitudinal analyses were performed to evaluate associations between group or dioxin and the change in the ratio of observed FEV_1 to observed FVC between the 1982 baseline examination and the 1997 follow-up.

18.2 RESULTS

18.2.1 Dependent Variable-Covariate Associations

Covariate tests of association were performed to examine the relations between the covariates used in the adjusted analyses and the dependent variables. Appendix F, Table F-10, provides summary results of these analyses to test the statistical significance of the associations. These associations are pairwise between the dependent variable and the covariate and are not adjusted for any other covariates. Participants with a pre-SEA occurrence of asthma were excluded from the analysis of asthma, and similar exclusions were made for bronchitis and pneumonia. Statistically significant associations are discussed below.

Covariate tests of association revealed no significant relations between asthma and any of the covariates ($p>0.70$ for all tests).

Analysis of bronchitis revealed significant covariate associations with lifetime cigarette smoking history ($p=0.002$) and industrial chemicals exposure ($p=0.009$), and a marginally significant association with race ($p=0.069$). The prevalence of bronchitis increased as lifetime cigarette smoking history increased. Participants who were exposed to industrial chemicals had a higher prevalence of bronchitis than those who were not exposed (22.0% vs. 17.2%). Non-Black participants had a higher prevalence of bronchitis than did Black participants (20.6% vs. 13.5%).

Covariate association tests for pneumonia revealed significant associations with age ($p=0.002$) and lifetime cigarette smoking history ($p=0.037$). Older participants had a higher percentage of pneumonia than did the younger participants (13.1% vs. 8.6%). Participants with greater than 10 pack-years had the highest prevalence of pneumonia (13.0%), followed by nonsmokers (9.6%) and participants between 0 and 10 pack-years (9.3%).

Tests of covariate association for thorax and lung abnormalities showed age ($p=0.001$), race ($p=0.042$), occupation ($p=0.001$), current cigarette smoking ($p=0.001$), lifetime cigarette smoking history ($p=0.001$), and body fat ($p=0.047$) to be significant. Exposure to industrial chemicals showed a marginally significant association with thorax and lung abnormalities ($p=0.062$). Older participants had a higher percentage of thorax and lung abnormalities (13.6%) than did the younger participants (8.6%). Non-Blacks had a higher prevalence of thorax and lungs abnormalities (11.8%) than did Blacks (5.5%). Enlisted flyers had the highest prevalence of abnormalities of the thorax and lung (18.6%), followed by

enlisted groundcrew (12.1%) and officers (7.7%). For both current cigarette smoking and lifetime cigarette smoking history, the prevalence of thorax and lung abnormalities increased as smoking increased. Participants with normal body fat had a higher percentage of thorax and lung abnormalities than obese participants (12.3% vs. 9.2%). Participants who had been exposed to industrial chemicals had a higher percentage of thorax and lung abnormalities (12.5%) than did participants who had not been exposed to industrial chemicals (9.7%).

Covariate association tests for the interpretation of the chest x ray revealed significant associations with age and lifetime cigarette smoking history (p=0.018 for both). Older participants had a higher percentage of x-ray interpretations showing abnormalities than did the younger participants (11.6% vs. 8.4%). The prevalence of x-ray interpretations showing abnormalities increased as lifetime cigarette smoking history increased.

For both current cigarette smoking and lifetime cigarette smoking history, FVC decreased significantly as smoking increased (p=0.002 for current cigarette smoking and p<0.001 for lifetime cigarette smoking history). FVC decreased significantly as body fat increased (p<0.001). Black participants had a lower mean FVC than did non-Black participants (87.84 vs. 99.81 percent of predicted, p<0.001). Occupation showed a significant association with FVC (p=0.005). Enlisted groundcrew had the lowest mean FVC (97.99 percent), followed by enlisted flyers (99.22 percent) and officers (100.28 percent).

FEV_1 decreased significantly with age (p<0.001), current cigarette smoking (p<0.001), lifetime cigarette smoking history (p<0.001), and body fat (p=0.001). Black participants had a lower mean FEV_1 than did non-Black participants (86.63 vs. 94.71 percent of predicted, p<0.001). Occupation showed a significant association with FEV_1 (p=0.002). Enlisted flyers had the lowest mean FEV_1 (91.76 percent), followed by enlisted groundcrew (93.90 percent) and officers (95.57 percent). The association between FEV_1 and exposure to industrial chemicals was marginally significant (p=0.092). The mean FEV_1 for participants not exposed to industrial chemicals was 95.04 percent, whereas the mean FEV_1 for participants exposed to industrial chemicals was 93.72 percent.

Because of the distribution of the data, a natural logarithm transformation of 1.0 minus the ratio of the observed FEV_1 to the observed FVC ratio was used. Because of this transformation, a negative correlation implies a positive association between dioxin and the ratio. The ratio of the observed FEV_1 to the observed FVC displayed significant associations with age, race, occupation, current cigarette smoking, lifetime cigarette smoking history, and body fat (p<0.001 for each). The ratio decreased with age, current cigarette smoking, and lifetime cigarette smoking history, but increased as body fat increased. Black participants had a higher mean ratio of the observed FEV_1 to the observed FVC than did non-Black participants (0.791 vs. 0.760). Enlisted groundcrew had the highest mean ratio (0.771), followed by officers (0.759) and enlisted flyers (0.745).

Tests of covariate association for loss of vital capacity showed a significant association with age (p=0.031), race (p=0.001), body fat (p=0.001), and lifetime cigarette smoking history (p=0.029). The association between loss of vital capacity and exposure to industrial chemicals was marginally significant (p=0.064). A higher percentage of older participants had a mild loss of vital capacity and a moderate or severe loss of vital capacity (mild: 8.4%, moderate or severe: 1.9%) than did younger participants (mild: 7.0%, moderate or severe: 0.8%). A higher percentage of Black participants had a mild loss of vital capacity and a moderate or severe loss of vital capacity (mild: 17.2%, moderate or severe: 4.7%) than did non-Blacks (mild: 7.2%, moderate or severe: 1.2%). Obese participants had a higher percentage of loss of vital capacity (mild: 11.9%, moderate or severe: 2.3%) than did those with normal body fat (mild: 6.1%, moderate or severe: 1.1%). Results also indicate that the percentage of mild loss of vital capacity and a moderate or severe loss of vital capacity increased as the number of pack-years increased. A higher percentage of participants exposed to industrial chemicals had a mild and moderate or severe loss of vital

capacity (mild: 8.5%, moderate or severe: 1.7%) than did participants not exposed to industrial chemicals (mild: 6.6%, moderate or severe: 0.9%).

Covariate analysis with obstructive abnormality revealed significant associations with age, occupation, current cigarette smoking, and lifetime cigarette smoking history (p=0.001 for each). Older participants had a higher percentage of obstructive abnormalities (mild: 37.1%, moderate: 8.6%, severe: 2.2%) than did younger participants (mild: 21.9%, moderate: 2.6%, severe: 0.4%). Enlisted flyers had a higher percentage of obstructive abnormalities than did officers or enlisted groundcrew. The percentage of obstructive abnormalities increased as the number of cigarettes smoked per day increased and as the number of pack-years increased.

18.2.2 Exposure Analysis

The following section presents results of the statistical analyses of the dependent variables shown in Table 18-1. Asthma, bronchitis, and pneumonia were derived from self-reported responses and verified by a medical records review. Additional dependent variables were taken from results of the physical examination and laboratory portions of the 1997 follow-up examination.

Four models were examined for each dependent variable given in Table 18-1. The analyses of these models are presented below. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7, respectively. These analyses were performed both unadjusted and adjusted for relevant covariates. Model 1 examined the relation between the dependent variable and group (i.e., Ranch Hand or Comparison). In this model, exposure was defined as "yes" for Ranch Hands and "no" for Comparisons without regard to the magnitude of the exposure. As an attempt to quantify exposure, three contrasts of Ranch Hands and Comparisons were performed along with the overall Ranch Hand versus Comparison contrast. These three contrasts compared Ranch Hands and Comparisons within each occupational category (i.e., officers, enlisted flyers, and enlisted groundcrew). As described in previous reports and Table 2-8, the average levels of exposure to dioxin were highest for enlisted groundcrew, followed by enlisted flyers, then officers.

Model 2 explored the relation between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt. If a participant did not have a 1987 dioxin level, the 1992 level was used to estimate the initial dioxin level. If a participant did not have a 1987 or a 1992 dioxin level, the 1997 level was used to estimate the initial dioxin level. A statistical adjustment for the percentage of body fat at the time of the participant's blood measurement of dioxin was included in this model to account for body-fat-related differences in elimination rate (43).

Model 3 divided the Ranch Hands examined in Model 2 into two categories based on their initial dioxin measures. These two categories are referred to as "low Ranch Hand" and "high Ranch Hand." Two additional categories, Ranch Hands with 1987 serum dioxin levels at or below 10 ppt and Comparisons with 1987 serum dioxin levels at or below 10 ppt, were formed and included in the model. Ranch Hands with 1987 serum dioxin levels at or below 10 ppt are referred to as the "background Ranch Hand" category. Dioxin levels in 1992 were used if the 1987 level was not available, and dioxin levels in 1997 were used if the 1987 and 1992 levels were not available. These four categories—Comparisons, background Ranch Hands, low Ranch Hands, and high Ranch Hands—were used in Model 3 analyses. The relation between the dependent variable in each of the three Ranch Hand categories and the dependent variable in the Comparison category was examined. A fourth contrast, exploring the relation of the dependent variable in the combined low and high Ranch Hand categories relative to Comparisons, also was conducted. This combination is referred to in the tables as the "low plus high Ranch Hand"

category. As in Model 2, a statistical adjustment for the percentage of body fat at the time of the participant's blood measurement of dioxin was included in this model.

Model 4 examined the relation between the dependent variable and 1987 lipid-adjusted dioxin levels in all Ranch Hands with a dioxin measurement. If a participant did not have a 1987 dioxin measurement, the 1992 measurement was used to determine the dioxin level. If a participant did not have a 1987 or a 1992 dioxin measurement, the 1997 measurement was used to determine the dioxin level.

18.2.2.1 Medical Records Variables

18.2.2.1.1 Asthma

All unadjusted and adjusted analyses of asthma for Models 1 through 4 were nonsignificant (Table 18-3(a–h): p>0.11 for all analyses).

Table 18-3. Analysis of Asthma

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***859***	***41 (4.8)***	***1.37 (0.89,2.11)***	***0.158***
	Comparison	***1,246***	***44 (3.5)***		
Officer	Ranch Hand	338	18 (5.3)	1.57 (0.80,3.10)	0.191
	Comparison	492	17 (3.5)		
Enlisted Flyer	Ranch Hand	149	3 (2.0)	0.46 (0.12,1.76)	0.257
	Comparison	187	8 (4.3)		
Enlisted Groundcrew	Ranch Hand	372	20 (5.4)	1.64 (0.86,3.11)	0.132
	Comparison	567	19 (3.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.36 (0.87,2.10)***	***0.175***
Officer	1.48 (0.74,2.94)	0.266
Enlisted Flyer	0.45 (0.12,1.74)	0.247
Enlisted Groundcrew	1.69 (0.89,3.21)	0.111

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	156	8 (5.1)	1.18 (0.86,1.62)	0.318
Medium	161	4 (2.5)		
High	158	9 (5.7)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 18-3. Analysis of Asthma (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
474	1.22 (0.82,1.82)	0.328

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,208	42 (3.5)		
Background RH	377	19 (5.0)	1.47 (0.84,2.58)	0.174
Low RH	235	10 (4.3)	1.23 (0.61,2.50)	0.559
High RH	240	11 (4.6)	1.33 (0.67,2.64)	0.408
Low plus High RH	475	21 (4.4)	1.28 (0.75,2.19)	0.363

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,207		
Background RH	376	1.52 (0.86,2.70)	0.149
Low RH	234	1.13 (0.54,2.36)	0.753
High RH	240	1.29 (0.64,2.61)	0.479
Low plus High RH	474	1.21 (0.69,2.10)	0.506

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 18-3. Analysis of Asthma (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	285	12 (4.2)	1.06 (0.86,1.31)	0.594
Medium	282	15 (5.3)		
High	285	13 (4.6)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
850	1.06 (0.81,1.37)	0.680

[a] Relative risk for a twofold increase in 1987 dioxin.

18.2.2.1.2 Bronchitis

The unadjusted and adjusted Model 1 analyses of bronchitis showed no difference between Ranch Hands and Comparisons when all occupations were combined (Table 18-4(a,b): p=0.177, unadjusted; p=0.213, adjusted). After stratifying by occupation, a marginally significant association was revealed between enlisted flyer Ranch Hands and enlisted flyer Comparisons in both the unadjusted and adjusted analyses (Table 18-4(a,b): Est. RR=1.63, p=0.066, for the unadjusted analysis; Adj. RR=1.61, p=0.075, for the adjusted analysis). The percentage of Ranch Hand enlisted flyers with bronchitis was 27.8, as compared to 19.1 percent of the Comparison enlisted flyers. Contrasts of Ranch Hands and Comparisons in the other occupations were nonsignificant (Table 18-4(a,b): p>0.49 for all analyses).

Table 18-4. Analysis of Bronchitis

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***846***	***183 (21.6)***	***1.16 (0.94,1.44)***	***0.177***
	Comparison	***1,224***	***235 (19.2)***		
Officer	Ranch Hand	329	60 (18.2)	1.03 (0.71,1.48)	0.886
	Comparison	482	86 (17.8)		
Enlisted Flyer	Ranch Hand	144	40 (27.8)	1.63 (0.97,2.73)	0.066
	Comparison	183	35 (19.1)		
Enlisted Groundcrew	Ranch Hand	373	83 (22.3)	1.12 (0.81,1.54)	0.496
	Comparison	559	114 (20.4)		

Table 18-4. Analysis of Bronchitis (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.15 (0.92,1.43)***	***0.213***
Officer	1.02 (0.70,1.47)	0.936
Enlisted Flyer	1.61 (0.95,2.71)	0.075
Enlisted Groundcrew	1.11 (0.81,1.54)	0.514

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	150	33 (22.0)	1.06 (0.89,1.25)	0.513
Medium	161	29 (18.0)		
High	156	36 (23.1)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
466	1.07 (0.88,1.30)	0.510

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,188	230 (19.4)		
Background RH	372	84 (22.6)	1.22 (0.92,1.62)	0.174
Low RH	228	44 (19.3)	1.00 (0.70,1.43)	0.980
High RH	239	54 (22.6)	1.21 (0.87,1.70)	0.262
Low plus High RH	467	98 (21.0)	1.10 (0.84,1.44)	0.479

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 18-4. Analysis of Bronchitis (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,187		
Background RH	371	1.31 (0.98,1.75)	0.073
Low RH	227	0.94 (0.65,1.36)	0.734
High RH	239	1.10 (0.78,1.56)	0.584
Low plus High RH	466	1.02 (0.78,1.34)	0.891

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	282	63 (22.3)	0.97 (0.87,1.08)	0.579
Medium	274	56 (20.4)		
High	283	63 (22.3)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
837	0.90 (0.79,1.03)	0.137

[a] Relative risk for a twofold increase in 1987 dioxin.

Models 2 and 4 showed no significant associations between dioxin and bronchitis (Table 18-4(c,d,g,h): p>0.13 for all analyses).

The unadjusted Model 3 analysis results of bronchitis were nonsignificant (Table 18-4(e): p>0.17 for each contrast). Adjusting for covariates revealed a marginally significant difference between Ranch Hands in the background dioxin category and Comparisons (Table 18-4(f): Adj. RR=1.31, p=0.073). The percentage of Ranch Hands with bronchitis in the background dioxin category was 22.6, versus 19.4 percent in the Comparison category.

18.2.2.1.3 Pneumonia

All unadjusted and adjusted Models 1, 3, and 4 analyses of pneumonia showed no significant results (Table 18-5(a,b,e–h): p>0.10 for all analyses).

Table 18-5. Analysis of Pneumonia

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***826***	***85 (10.3)***	***0.87 (0.66,1.16)***	***0.344***
	Comparison	***1,204***	***140 (11.6)***		
Officer	Ranch Hand	322	34 (10.6)	0.75 (0.48,1.17)	0.200
	Comparison	470	64 (13.6)		
Enlisted Flyer	Ranch Hand	139	19 (13.7)	1.74 (0.85,3.57)	0.129
	Comparison	180	15 (8.3)		
Enlisted Groundcrew	Ranch Hand	365	32 (8.8)	0.78 (0.50,1.22)	0.271
	Comparison	554	61 (11.0)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.87 (0.66,1.16)***	***0.354***
Officer	0.74 (0.47,1.16)	0.185
Enlisted Flyer	1.75 (0.85,3.61)	0.126
Enlisted Groundcrew	0.79 (0.50,1.24)	0.304

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	147	21 (14.3)	0.81 (0.63,1.05)	0.097
Medium	156	12 (7.7)		
High	155	13 (8.4)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

n	Analysis Results for Log_2 (Initial Dioxin) Adjusted Relative Risk (95% C.I.)[a]	p-Value
457	0.85 (0.63,1.14)	0.274

[a] Relative risk for a twofold increase in initial dioxin.

Table 18-5. Analysis of Pneumonia (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,168	134 (11.5)		
Background RH	361	38 (10.5)	0.93 (0.63,1.36)	0.708
Low RH	222	27 (12.2)	1.06 (0.68,1.65)	0.790
High RH	236	19 (8.1)	0.66 (0.40,1.09)	0.107
Low plus High RH	458	46 (10.0)	0.83 (0.58,1.19)	0.315

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,167		
Background RH	360	0.90 (0.61,1.33)	0.602
Low RH	221	0.98 (0.63,1.54)	0.929
High RH	236	0.74 (0.44,1.25)	0.265
Low plus High RH	457	0.85 (0.59,1.23)	0.386

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Yes	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	269	29 (10.8)	0.91 (0.78,1.07)	0.236
Medium	270	33 (12.2)		
High	280	22 (7.9)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 18-5. Analysis of Pneumonia (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
817	0.89 (0.73,1.08)	0.229

[a] Relative risk for a twofold increase in 1987 dioxin.

The unadjusted Model 2 analysis found a marginally significant relation between pneumonia and initial dioxin (Table 18-5(c): Est. RR=0.81, p=0.097). As initial dioxin increased, the prevalence of pneumonia decreased. The percentages of Ranch Hands with pneumonia in the low, medium, and high initial dioxin categories were 14.3, 7.7, and 8.4, respectively. After adjustment for covariates, the association was nonsignificant (Table 18-5(d): p=0.274).

18.2.2.2 Physical Examination Variable

18.2.2.2.1 Thorax and Lung Abnormalities

Results from the unadjusted and adjusted Models 1 through 3 analyses of thorax and lung abnormalities were nonsignificant (Table 18-6(a–f): p≥0.11 for each analysis).

Table 18-6. Analysis of Thorax and Lung Abnormalities

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***870***	***102 (11.7)***	***1.05 (0.80,1.38)***	***0.704***
	Comparison	***1,251***	***140 (11.2)***		
Officer	Ranch Hand	341	31 (9.1)	1.40 (0.84,2.33)	0.200
	Comparison	494	33 (6.7)		
Enlisted Flyer	Ranch Hand	151	29 (19.2)	1.07 (0.62,1.85)	0.810
	Comparison	187	34 (18.2)		
Enlisted Groundcrew	Ranch Hand	378	42 (11.1)	0.85 (0.57,1.27)	0.434
	Comparison	570	73 (12.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***0.97 (0.71,1.31)***	***0.821***
Officer	1.57 (0.90,2.71)	0.110
Enlisted Flyer	0.99 (0.53,1.85)	0.978
Enlisted Groundcrew	0.69 (0.44,1.09)	0.115

Table 18-6. Analysis of Thorax and Lung Abnormalities (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log₂ (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Number (%) Yes**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	160	22 (13.8)	1.06 (0.86,1.31)	0.573
Medium	162	23 (14.2)		
High	160	17 (10.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
481	1.14 (0.86,1.51)	0.366

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	**n**	**Number (%) Yes**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,213	137 (11.3)		
Background RH	381	39 (10.2)	0.82 (0.56,1.20)	0.304
Low RH	239	31 (13.0)	1.19 (0.79,1.82)	0.408
High RH	243	31 (12.8)	1.24 (0.82,1.89)	0.313
Low plus High RH	482	62 (12.9)	1.22 (0.88,1.68)	0.232

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 18-6. Analysis of Thorax and Lung Abnormalities (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Comparison	1,212		
Background RH	380	0.84 (0.55,1.28)	0.412
Low RH	238	1.01 (0.63,1.62)	0.953
High RH	243	1.01 (0.62,1.64)	0.977
Low plus High RH	481	1.01 (0.70,1.46)	0.955

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**	
1987 Dioxin	**n**	**Number (%) Yes**	**Estimated Relative Risk (95% C.I.)[a]**	**p-Value**
Low	288	32 (11.1)	1.03 (0.90,1.19)	0.653
Medium	287	31 (10.8)		
High	288	38 (13.2)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
861	1.20 (1.00,1.43)	0.054

[a] Relative risk for a twofold increase in 1987 dioxin.

The unadjusted Model 4 analysis was nonsignificant (Table 18-6(g): p=0.653). After adjusting for covariates, a marginally significant association between thorax and lung abnormalities and 1987 dioxin was revealed (Table 18-6(h): Adj. RR=1.20, p=0.054). As 1987 dioxin increased, the prevalence of thorax and lung abnormalities increased. The percentages of Ranch Hands with thorax and lung abnormalities in the low, medium, and high 1987 dioxin categories were 11.1, 10.8, and 13.2, respectively.

18.2.2.3 Laboratory Examination Variables

18.2.2.3.1 X-ray Interpretation

All unadjusted and adjusted analyses of the chest x-ray interpretation for Models 1 and 2 were nonsignificant (Table 18-7(a–d): p>0.15 for each analysis).

Table 18-7. Analysis of X-ray Interpretation

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***868***	***98 (11.3)***	***1.22 (0.92,1.62)***	***0.166***
	Comparison	***1,251***	***118 (9.4)***		
Officer	Ranch Hand	341	39 (11.4)	1.39 (0.88,2.20)	0.160
	Comparison	494	42 (8.5)		
Enlisted Flyer	Ranch Hand	151	16 (10.6)	1.19 (0.58,2.43)	0.643
	Comparison	187	17 (9.1)		
Enlisted Groundcrew	Ranch Hand	376	43 (11.4)	1.12 (0.74,1.70)	0.599
	Comparison	570	59 (10.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.23 (0.92,1.64)***	***0.158***
Officer	1.39 (0.87,2.20)	0.167
Enlisted Flyer	1.16 (0.56,2.39)	0.685
Enlisted Groundcrew	1.14 (0.75,1.73)	0.554

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	18 (11.3)	0.89 (0.70,1.15)	0.373
Medium	161	14 (8.7)		
High	159	11 (6.9)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 18-7. Analysis of X-ray Interpretation (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
479	0.95 (0.71,1.27)	0.730

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,213	116 (9.6)		
Background RH	381	53 (13.9)	1.56 (1.10,2.21)	0.013
Low RH	239	26 (10.9)	1.15 (0.73,1.80)	0.546
High RH	241	17 (7.1)	0.70 (0.41,1.20)	0.196
Low plus High RH	480	43 (9.0)	0.90 (0.62,1.31)	0.576

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED			
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,212		
Background RH	380	1.69 (1.18,2,43)	0.004
Low RH	238	1.11 (0.70,1.75)	0.657
High RH	241	0.66 (0.38,1.13)	0.127
Low plus High RH	479	0.85 (0.58,1.24)	0.406

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 18-7. Analysis of X-ray Interpretation (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	37 (12.8)	0.83 (0.71,0.97)	0.015
Medium	287	39 (13.6)		
High	286	20 (7.0)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
Analysis Results for Log_2 (1987 Dioxin + 1)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
859	0.80 (0.67,0.96)	0.015

[a] Relative risk for a twofold increase in 1987 dioxin.

In the Model 3 unadjusted analysis of the x-ray interpretation, a significant difference was revealed between Ranch Hands in the background dioxin category and Comparisons (Table 18-7(e): Est. RR=1.56, p=0.013). The percentage of Ranch Hands in the background dioxin category with an x ray showing abnormalities was 13.9 percent, versus 9.6 percent of Comparisons. The same contrast was significant in the adjusted analysis (Table 18-7(f): Adj. RR=1.69, p=0.004). Unadjusted and adjusted contrasts of the low, high, and low plus high dioxin Ranch Hand categories with Comparisons were all nonsignificant (Table 18-7(e,f): p>0.12 for all analyses).

Both the unadjusted and adjusted Model 4 analyses revealed significant associations between the x-ray interpretation and 1987 dioxin (Table 18-7(g,h): Est. RR=0.83, p=0.015; Adj. RR=0.80, p=0.015, respectively). As the 1987 dioxin level increased, the prevalence of an x ray showing abnormalities decreased. The percentages of participants with an x-ray interpretation showing abnormalities in the low, medium, and high 1987 dioxin categories were 12.8, 13.6, and 7.0, respectively.

18.2.2.3.2 FVC (Percent of Predicted)

All unadjusted and adjusted analyses of the FVC were nonsignificant (Table 18-8: p>0.32 for all analyses).

Table 18-8. Analysis of FVC (Percent of Predicted)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean	Difference of Means (95% C.I.)	p-Value
All	*Ranch Hand*	*869*	*99.31*	*0.38 (–0.91,1.68)*	*0.564*
	Comparison	*1,249*	*98.93*		
Officer	Ranch Hand	341	100.48	0.33 (–1.73,2.39)	0.753
	Comparison	494	100.14		
Enlisted Flyer	Ranch Hand	151	99.64	0.75 (–2.45,3.96)	0.645
	Comparison	186	98.88		
Enlisted Groundcrew	Ranch Hand	377	98.14	0.24 (–1.71,2.18)	0.811
	Comparison	569	97.90		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean	Difference of Adj. Means (95% C.I.)	p-Value
All	*Ranch Hand*	*867*	*94.21*	*0.41 (–0.81,1.64)*	*0.506*
	Comparison	*1,248*	*93.79*		
Officer	Ranch Hand	340	94.31	0.56 (–1.39,2.50)	0.575
	Comparison	494	93.76		
Enlisted Flyer	Ranch Hand	151	95.01	0.56 (–2.47,3.59)	0.716
	Comparison	186	94.45		
Enlisted Groundcrew	Ranch Hand	376	93.36	0.23 (–1.61,2.07)	0.804
	Comparison	568	93.12		

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Mean	Adj. Mean[a]	R^2	Slope (Std. Error)	p-Value
Low	160	98.34	98.13	0.018	0.332 (0.491)	0.499
Medium	161	97.80	97.76			
High	160	99.44	99.68			

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean	R^2	Adj. Slope (Std. Error)	p-Value
Low	159	95.17	0.099	–0.303 (0.558)	0.588
Medium	161	94.32			
High	160	95.09			

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 18-8. Analysis of FVC (Percent of Predicted) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,211	99.09	99.14		
Background RH	381	100.18	99.33	0.19 (–1.50,1.88)	0.825
Low RH	238	98.07	98.34	–0.80 (–2.83,1.23)	0.439
High RH	243	98.97	99.79	0.66 (–1.36,2.67)	0.523
Low plus High RH	481	98.52	99.07	–0.06 (–1.61,1.48)	0.935

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,210	93.87		
Background RH	380	93.72	–0.15 (–1.80,1.50)	0.859
Low RH	237	94.29	0.42 (–1.54,2.39)	0.674
High RH	243	94.61	0.75 (–1.25,2.74)	0.465
Low plus High RH	480	94.45	0.59 (–0.92,2.09)	0.445

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean	R^2	Slope (Std. Error)	p-Value
Low	288	100.86	0.001	–0.312 (0.338)	0.356
Medium	287	98.03			
High	287	98.86			

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 18-8. Analysis of FVC (Percent of Predicted) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean	R^2	Adjusted Slope (Std. Error)	p-Value
Low	287	94.50	0.111	0.377 (0.385)	0.329
Medium	286	94.05			
High	287	95.18			

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

18.2.2.3.3 FEV_1 (Percent of Predicted)

No significant relations were observed between group or dioxin and FEV_1 in any of the analyses (Table 18-9(a–h): p>0.13 for all analyses).

Table 18-9. Analysis of FEV_1 (Percent of Predicted)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean	Difference of Means (95% C.I.)	p-Value
All	***Ranch Hand***	***869***	***94.13***	***–0.15 (–1.66,1.37)***	***0.849***
	Comparison	***1,249***	***94.28***		
Officer	Ranch Hand	341	95.47	–0.18 (–2.58,2.23)	0.886
	Comparison	494	95.65		
Enlisted Flyer	Ranch Hand	151	91.09	–1.21 (–4.95,2.54)	0.527
	Comparison	186	92.30		
Enlisted Groundcrew	Ranch Hand	377	94.14	0.40 (–1.87,2.67)	0.729
	Comparison	569	93.74		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED					
Occupational Category	Group	n	Adjusted Mean	Difference of Adj. Means (95% C.I.)	p-Value
All	***Ranch Hand***	***867***	***90.23***	***0.17 (–1.24,1.57)***	***0.814***
	Comparison	***1,248***	***90.06***		
Officer	Ranch Hand	340	90.92	0.11 (–2.13,2.35)	0.925
	Comparison	494	90.81		
Enlisted Flyer	Ranch Hand	151	89.19	–1.27 (–4.75,2.21)	0.475
	Comparison	186	90.46		
Enlisted Groundcrew	Ranch Hand	376	90.07	0.75 (–1.36,2.87)	0.484
	Comparison	568	89.32		

Table 18-9. Analysis of FEV_1 (Percent of Predicted) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Mean	Adj. Mean[a]	R^2	Slope (Std. Error)	p-Value
Low	160	93.08	93.14	0.006	0.870 (0.581)	0.135
Medium	161	91.83	91.84			
High	160	97.27	97.20			

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean	R^2	Adj. Slope (Std. Error)	p-Value
Low	159	91.50	0.143	0.007 (0.637)	0.991
Medium	161	90.10			
High	160	93.52			

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,211	94.36	94.38		
Background RH	381	94.17	93.94	–0.44 (–2.46,1.57)	0.668
Low RH	238	92.82	92.89	–1.48 (–3.90,0.93)	0.229
High RH	243	95.27	95.50	1.12 (–1.28,3.53)	0.360
Low plus High RH	481	94.06	94.21	–0.17 (–2.01,1.67)	0.859

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 18-9. Analysis of FEV₁ (Percent of Predicted) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	**n**	**Adj. Mean**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)**	**p-Value**
Comparison	1,210	90.03		
Background RH	380	89.32	–0.70 (–2.59,1.19)	0.469
Low RH	237	90.58	0.55 (–1.70,2.80)	0.632
High RH	243	91.19	1.16 (–1.13,3.45)	0.319
Low plus High RH	480	90.89	0.86 (–0.86,2.58)	0.328

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin +1)**		
1987 Dioxin	**n**	**Mean**	**R^2**	**Slope (Std. Error)**	**p-Value**
Low	288	94.88	0.002	0.496 (0.402)	0.217
Medium	287	92.76			
High	287	94.69			

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**		
1987 Dioxin	**n**	**Adj. Mean**	**R^2**	**Adjusted Slope (Std. Error)**	**p-Value**
Low	287	89.98	0.161	0.652 (0.443)	0.142
Medium	286	89.99			
High	287	91.21			

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

18.2.2.3.4 Ratio of Observed FEV_1 to Observed FVC

Because of the distribution of the data, a natural logarithm transformation of 1.0 minus the ratio was used. Because of this transformation, a negative slope in Models 2 and 4 implies a positive association between dioxin and the ratio of observed FEV_1 to FVC. A negative association, which would be represented by a positive slope, is considered adverse for this variable.

Model 1 showed no significant difference between Ranch Hands and Comparisons in the mean ratio of observed FEV_1 to observed FVC (Table 18-10(a,b): $p>0.36$ for each contrast).

The Model 2 unadjusted analysis showed a significant positive association between the ratio of observed FEV_1 to observed FVC and initial dioxin (Table 18-10(c): slope=–0.026, p=0.023). The mean ratios in

the low, medium, and high initial dioxin categories were 0.759, 0.756, and 0.783, respectively. The adjusted analysis was nonsignificant (Table 18-10(d): p=0.360).

The Model 3 unadjusted and adjusted analyses showed no significant difference between any of the Ranch Hand dioxin categories and the Comparison group (Table 18-10(e,f): p>0.16 for each contrast).

The unadjusted Model 4 analysis found a significant positive association between 1987 dioxin and the ratio of observed FEV_1 to observed FVC (slope=–0.031, p<0.001). The mean ratios in the low, medium, and high 1987 dioxin categories were 0.753, 0.757, and 0.771, respectively. After adjusting for covariates, the results were nonsignificant (p=0.161).

Table 18-10. Analysis of the Ratio of Observed FEV_1 to Observed FVC

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***869***	***0.760***	***–0.003 --***	***0.366***
	Comparison	***1,249***	***0.763***		
Officer	Ranch Hand	341	0.756	–0.005 --	0.376
	Comparison	494	0.761		
Enlisted Flyer	Ranch Hand	151	0.741	–0.007 --	0.431
	Comparison	186	0.748		
Enlisted Groundcrew	Ranch Hand	377	0.772	0.001 --	0.843
	Comparison	569	0.771		

[a] Transformed from natural logarithm scale of 1.0 – ratio.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale of 1.0 – ratio.
[c] P-value is based on difference of means on natural logarithm scale of 1.0 – ratio.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***867***	***0.770***	***–0.001 --***	***0.701***
	Comparison	***1,248***	***0.771***		
Officer	Ranch Hand	340	0.771	–0.004 --	0.411
	Comparison	494	0.775		
Enlisted Flyer	Ranch Hand	151	0.764	–0.005 --	0.486
	Comparison	186	0.770		
Enlisted Groundcrew	Ranch Hand	376	0.774	0.003 --	0.532
	Comparison	568	0.771		

[a] Transformed from natural logarithm scale of 1.0 – ratio.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale of 1.0 – ratio.
[c] P-value is based on difference of means on natural logarithm scale of 1.0 – ratio.

Table 18-10. Analysis of the Ratio of Observed FEV$_1$ to Observed FVC (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	160	0.757	0.759	0.053	–0.026 (0.011)	0.023
Medium	161	0.756	0.756			
High	160	0.785	0.783			

[a] Transformed from natural logarithm scale of 1.0 – ratio.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of (1.0 – ratio) versus log$_2$ (initial dioxin); because of this transformation, a negative slope implies a positive association between the ratio and log$_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED					
Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	159	0.773	0.216	–0.011 (0.012)	0.360
Medium	161	0.770			
High	160	0.788			

[a] Transformed from natural logarithm scale of 1.0 – ratio.
[b] Slope and standard error based on natural logarithm of (1.0 – ratio) versus log$_2$ (initial dioxin); because of this transformation, a negative slope implies a positive association between the ratio and log$_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,211	0.763	0.763		
Background RH	381	0.753	0.757	–0.006 --	0.192
Low RH	238	0.759	0.757	–0.006 --	0.341
High RH	243	0.774	0.770	0.007 --	0.164
Low plus High RH	481	0.766	0.764	0.001 --	0.764

[a] Transformed from natural logarithm scale of 1.0 – ratio.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale of 1.0 – ratio.
[d] P-value is based on difference of means on natural logarithm scale of 1.0 – ratio.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 18-10. Analysis of the Ratio of Observed FEV_1 to Observed FVC (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,210	0.770		
Background RH	380	0.766	–0.004 --	0.376
Low RH	237	0.772	0.002 --	0.740
High RH	243	0.774	0.004 --	0.466
Low plus High RH	480	0.773	0.003 --	0.481

[a] Transformed from natural logarithm scale of 1.0 – ratio.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale of 1.0 – ratio.
[c] P-value is based on difference of means on natural logarithm scale of 1.0 – ratio.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for $\log_2$ (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	288	0.753	0.018	–0.031 (0.008)	<0.001
Medium	287	0.757			
High	287	0.771			

[a] Transformed from natural logarithm scale of 1.0 – ratio.
[b] Slope and standard error based on natural logarithm of (1.0 – ratio) versus $\log_2$ (1987 dioxin + 1); because of this transformation, a negative slope implies a positive association between the ratio and $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for $\log_2$ (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	287	0.767	0.218	–0.012 (0.008)	0.161
Medium	286	0.770			
High	287	0.773			

[a] Transformed from natural logarithm scale of 1.0 – ratio.
[b] Slope and standard error based on natural logarithm of (1.0 – ratio) versus $\log_2$ (1987 dioxin + 1); because of this transformation, a negative slope implies a positive association between the ratio and $\log_2$ (1987 dioxin+1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

18.2.2.3.5 Loss of Vital Capacity

No significant relations were observed between group or dioxin and the loss of vital capacity in Models 1 through 3 (Table 18-11(a–f): p>0.11 for each analysis).

Table 18-11. Analysis of Loss of Vital Capacity

(a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

			Number (%)			Mild vs. None		Moderate or Severe vs. None	
Occupational Category	Group	n	None	Mild	Moderate or Severe	Est. Relative Risk (95% C.I.)	p-Value	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***869***	***792 (91.1)***	***67 (7.7)***	***10 (1.2)***	***0.98 (0.71,1.35)***	***0.885***	***0.71 (0.33,1.53)***	***0.388***
	Comparison	***1,249***	***1,131 (90.6)***	***98 (7.8)***	***20 (1.6)***				
Officer	Ranch Hand	341	312 (91.5)	24 (7.0)	5 (1.5)	1.10 (0.63,1.90)	0.737	1.46 (0.42,5.10)	0.549
	Comparison	494	457 (92.5)	32 (6.5)	5 (1.0)				
Enlisted Flyer	Ranch Hand	151	139 (92.1)	11 (7.3)	1 (0.7)	0.72 (0.33,1.58)	0.413	0.29 (0.03,2.67)	0.277
	Comparison	186	164 (88.2)	18 (9.7)	4 (2.2)				
Enlisted Groundcrew	Ranch Hand	377	341 (90.5)	32 (8.5)	4 (1.1)	1.00 (0.62,1.59)	0.990	0.54 (0.17,1.72)	0.300
	Comparison	569	510 (89.6)	48 (8.4)	11 (1.9)				

(b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

	Mild vs. None		Moderate or Severe vs. None	
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Adj. Relative Risk (95% C.I.)	p-Value
All	***0.96 (0.69,1.35)***	***0.832***	***0.67 (0.31,1.47)***	***0.324***
Officer	1.09 (0.62,1.90)	0.768	1.42 (0.40,5.00)	0.586
Enlisted Flyer	0.68 (0.31,1.52)	0.349	0.25 (0.03,2.30)	0.220
Enlisted Groundcrew	1.00 (0.61,1.63)	0.999	0.52 (0.16,1.70)	0.279

Table 18-11. Analysis of Loss of Vital Capacity (Continued)

(c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED								
Initial Dioxin Category Summary Statistics					Analysis Results for Log_2 (Initial Dioxin)[a]			
		Number (%)			Mild vs. None		Moderate or Severe vs. None	
Initial Dioxin Category	n	None	Mild	Moderate or Severe	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
Low	160	146 (91.3)	12 (7.5)	2 (1.3)	0.88 (0.67,1.15)	0.345	0.73 (0.31,1.76)	0.489
Medium	161	145 (90.1)	15 (9.3)	1 (0.6)				
High	160	151 (94.4)	8 (5.0)	1 (0.6)				

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Initial Dioxin)			
	Mild vs. None		Moderate or Severe vs. None	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
480	0.91 (0.66,1.24)	0.539	1.02 (0.35,2.99)	0.973

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results not adjusted for race, current cigarette smoking, and industrial chemicals exposure because of the sparse number of moderate or severe measurements.

Table 18-11. Analysis of Loss of Vital Capacity (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED								
		Number (%)			Mild vs. None		Moderate or Severe vs. None	
Dioxin Category	n	None	Mild	Moderate or Severe	Est. Relative Risk (95% C.I.)[ab]	p-Value	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	1,096 (90.5)	97 (8.0)	18 (1.5)				
Background RH	381	344 (90.3)	31 (8.1)	6 (1.6)	1.18 (0.77,1.81)	0.456	1.27 (0.50,3.27)	0.616
Low RH	238	218 (91.6)	18 (7.6)	2 (0.8)	0.89 (0.52,1.51)	0.663	0.52 (0.12,2.28)	0.387
High RH	243	224 (92.2)	17 (7.0)	2 (0.8)	0.75 (0.43,1.29)	0.295	0.46 (0.10,2.00)	0.297
Low plus High RH	481	442 (91.9)	35 (7.3)	4 (0.8)	0.81 (0.54,1.23)	0.325	0.49 (0.16,1.46)	0.199

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
		Mild vs. None		Moderate or Severe vs. None	
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,210				
Background RH	380	1.28 (0.82,1.99)	0.284	1.44 (0.54,3.81)	0.468
Low RH	237	0.71 (0.41,1.24)	0.235	0.34 (0.07,1.57)	0.165
High RH	243	0.75 (0.43,1.32)	0.325	0.47 (0.10,2.17)	0.337
Low plus High RH	480	0.73 (0.48,1.12)	0.151	0.40 (0.13,1.25)	0.115

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 18-11. Analysis of Loss of Vital Capacity (Continued)

(g) MODEL 4: RANCH HANDS — 1987 DIOXIN — UNADJUSTED								
1987 Dioxin Category Summary Statistics					Analysis Results for Log_2 (1987 Dioxin + 1)			
		Number (%)			Mild vs. None		Moderate or Severe vs. None	
1987 Dioxin Category	n	None	Mild	Moderate or Severe	Est. Relative Risk (95% C.I.)[a]	p-Value	Est. Relative Risk (95% C.I.)[a]	p-Value
Low	288	265 (92.0)	19 (6.6)	4 (1.4)	0.94 (0.79,1.12)	0.480	0.83 (0.53,1.31)	0.430
Medium	287	254 (88.5)	29 (10.1)	4 (1.4)				
High	287	267 (93.0)	18 (6.3)	2 (0.7)				

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS — 1987 DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (1987 Dioxin + 1)			
	Mild vs. None		Moderate or Severe vs. None	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
860	0.80 (0.65,1.00)	0.046	0.87 (0.50,1.50)	0.605

[a] Relative risk for a twofold increase in 1987 dioxin.

The Model 4 unadjusted analysis of loss of vital capacity was nonsignificant (Table 18-11(g): $p>0.43$ for each contrast). After adjusting for covariates, a significant association between a mild loss of vital capacity and 1987 dioxin was revealed (Table 18-11(h): Adj. RR=0.80, p=0.046). The prevalence of a mild loss of vital capacity decreased as 1987 dioxin increased, after accounting for covariate effects. The percentages of participants with a mild loss of vital capacity in the low, medium, and high 1987 dioxin categories were 6.6, 10.1, and 6.3, respectively.

18.2.2.3.6 Obstructive Abnormality

The Model 1 unadjusted and adjusted analyses showed no group difference for obstructive abnormalities when combining all occupations ($p>0.23$ for each analysis). After stratifying by occupation, both the unadjusted and adjusted analyses revealed a significant difference between Ranch Hand and Comparison officers in the percentage of mild obstructive abnormalities (Table 18-12(a,b): Est. RR=1.38, p=0.034; Adj. RR=1.38, p=0.041, respectively). The percentage of Ranch Hand officers with mild obstructive abnormalities was higher than the percentage of Comparison officers with mild obstructive abnormalities (36.4% vs. 29.8%). No significant differences were noted for any occupation for the contrast of moderate versus no obstructive abnormalities ($p>0.36$ for all analyses) or for the contrast of severe versus no obstructive abnormalities ($p\geq0.18$ for all analyses).

Table 18-12. Analysis of Obstructive Abnormality

(a1) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Number (%) None	Mild	Moderate	Severe
All	***Ranch Hand***	***869***	***528 (60.8)***	***276 (31.8)***	***51 (5.9)***	***14 (1.6)***
	Comparison	***1,249***	***790 (63.3)***	***368 (29.5)***	***75 (6.0)***	***16 (1.3)***
Officer	Ranch Hand	341	193 (56.6)	124 (36.4)	19 (5.6)	5 (1.5)
	Comparison	494	316 (64.0)	147 (29.8)	26 (5.3)	5 (1.0)
Enlisted Flyer	Ranch Hand	151	82 (54.3)	49 (32.5)	14 (9.3)	6 (4.0)
	Comparison	186	97 (52.2)	72 (38.7)	12 (6.5)	5 (2.7)
Enlisted Groundcrew	Ranch Hand	377	253 (67.1)	103 (27.3)	18 (4.8)	3 (0.8)
	Comparison	569	377 (66.3)	149 (26.2)	37 (6.5)	6 (1.1)

(a2) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Mild vs. None Est. Relative Risk (95% C.I.)	p-Value	Moderate vs. None Est. Relative Risk (95% C.I.)	p-Value	Severe vs. None Est. Relative Risk (95% C.I.)	p-Value
All	***1.12 (0.93,1.36)***	***0.237***	***1.02 (0.70,1.48)***	***0.928***	***1.31 (0.63,2.70)***	***0.467***
Officer	1.38 (1.02,1.86)	0.034	1.20 (0.64,2.22)	0.569	1.64 (0.47,5.73)	0.440
Enlisted Flyer	0.81 (0.50,1.28)	0.363	1.38 (0.60,3.15)	0.444	1.42 (0.42,4.82)	0.574
Enlisted Groundcrew	1.03 (0.77,1.39)	0.845	0.72 (0.40,1.30)	0.281	0.75 (0.18,3.00)	0.679

Table 18-12. Analysis of Obstructive Abnormality (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED						
	Mild vs. None		Moderate vs. None		Severe vs. None	
Occupational Category	Est. Relative Risk (95% C.I.)	p-Value	Est. Relative Risk (95% C.I.)	p-Value	Est. Relative Risk (95% C.I.)	p-Value
All	***1.08 (0.88,1.32)***	***0.449***	***0.97 (0.66,1.44)***	***0.887***	***1.22 (0.57,2.59)***	***0.605***
Officer	1.38 (1.01,1.89)	0.041	1.21 (0.63,2.32)	0.560	1.81 (0.50,6.57)	0.366
Enlisted Flyer	0.79 (0.48,1.29)	0.345	1.36 (0.57,3.23)	0.492	1.27 (0.35,4.58)	0.715
Enlisted Groundcrew	0.96 (0.70,1.32)	0.821	0.65 (0.35,1.22)	0.180	0.69 (0.16,2.87)	0.607

(c1) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED					
		Initial Dioxin Category Summary Statistics Number (%)			
Initial Dioxin Category	n	None	Mild	Moderate	Severe
Low	160	93 (58.1)	52 (32.5)	11 (6.9)	4 (2.5)
Medium	161	94 (58.4)	56 (34.8)	8 (5.0)	3 (1.9)
High	160	121 (75.6)	32 (20.0)	7 (4.4)	0 (0.0)

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(c2) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED					
Analysis Results for Log_2 (Initial Dioxin)[a]					
Mild vs. None		Moderate vs. None		Severe vs. None	
Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
0.79 (0.67,0.93)	0.005	0.87 (0.63,1.20)	0.393	0.53 (0.24,1.21)	0.131

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

(d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
	Analysis Results for Log_2 (Initial Dioxin)					
	Mild vs. None		Moderate vs. None		Severe vs. None	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
480	0.86 (0.72,1.02)	0.082	0.98 (0.67,1.42)	0.902	0.63 (0.28,1.44)	0.276

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results not adjusted for race, occupation, and industrial chemicals exposure because of the sparse number of severe obstructive abnormalities.

Table 18-12. Analysis of Obstructive Abnormality (Continued)

(e1) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED						
		Number (%)				
Dioxin Category	n	None	Mild	Moderate	Severe	
Comparison	1,211	767 (63.3)	356 (29.4)	73 (6.0)	15 (1.2)	
Background RH	381	218 (57.2)	131 (34.4)	25 (6.6)	7 (1.8)	
Low RH	238	134 (56.3)	85 (35.7)	13 (5.5)	6 (2.5)	
High RH	243	174 (71.6)	55 (22.6)	13 (5.3)	1 (0.4)	
Low plus High RH	481	308 (64.0)	140 (29.1)	26 (5.4)	7 (1.5)	

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(e2) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED						
	Mild vs. None		Moderate vs. None		Severe vs. None	
Dioxin Category	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)	p-Value
Comparison						
Background RH	1.26 (0.98,1.62)	0.071	1.14 (0.70,1.85)	0.595	1.42 (0.57,3.55)	0.453
Low RH	1.38 (1.02,1.86)	0.037	1.03 (0.56,1.92)	0.915	2.37 (0.90,6.24)	0.080
High RH	0.70 (0.50,0.97)	0.031	0.82 (0.44,1.52)	0.533	0.33 (0.04,2.56)	0.291
Low plus High RH	0.98 (0.77,1.24)	0.838	0.92 (0.58,1.47)	0.731	0.88 (0.27,2.90)	0.835

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 18-12. Analysis of Obstructive Abnormality (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED							
		Mild vs. None		Moderate vs. None		Severe vs. None	
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)	p-Value
Comparison	1,210						
Background RH	380	1.21 (0.93,1.58)	0.164	1.22 (0.73,2.04)	0.440	1.64 (0.62,4.34)	0.323
Low RH	237	1.17 (0.85,1.60)	0.338	0.78 (0.40,1.52)	0.459	1.75 (0.62,4.89)	0.289
High RH	243	0.74 (0.52,1.06)	0.096	0.76 (0.39,1.49)	0.429	0.28 (0.03,2.26)	0.232
Low plus High RH	480	0.93 (0.72,1.20)	0.556	0.77 (0.46,1.28)	0.311	0.69 (0.20,2.37)	0.557

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g1) MODEL 4: RANCH HANDS — 1987 DIOXIN — UNADJUSTED					
		1987 Dioxin Category Summary Statistics Number (%)			
1987 Dioxin Category	n	None	Mild	Moderate	Severe
Low	288	168 (58.3)	97 (33.7)	17 (5.9)	6 (2.1)
Medium	287	161 (56.1)	101 (35.2)	20 (7.0)	5 (1.7)
High	287	197 (68.6)	73 (25.4)	14 (4.9)	3 (1.0)

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(g2) MODEL 4: RANCH HANDS — 1987 DIOXIN — UNADJUSTED					
Analysis Results for Log_2 (1987 Dioxin+1)					
Mild vs. None		Moderate vs. None		Severe vs. None	
Est. Relative Risk (95% C.I.)[a]	p-Value	Est. Relative Risk (95% C.I.)[a]	p-Value	Est. Relative Risk (95% C.I.)[a]	p-Value
0.83 (0.75,0.92)	<0.001	0.86 (0.70,1.05)	0.145	0.70 (0.47,1.04)	0.078

[a] Relative risk for a twofold increase in 1987 dioxin.

(h) MODEL 4: RANCH HANDS — 1987 DIOXIN — ADJUSTED						
	Analysis Results for Log_2 (1987 Dioxin+1)					
	Mild vs. None		Moderate vs. None		Severe vs. None	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
860	0.91 (0.80,1.04)	0.177	0.87 (0.67,1.12)	0.269	0.78 (0.50,1.22)	0.272

[a] Relative risk for a twofold increase in 1987 dioxin.

In each of the unadjusted and adjusted Model 2 analyses, a significant or marginally significant decreased risk of mild obstructive abnormalities for increasing initial dioxin levels was revealed (Table 18-12(c,d): Est. RR=0.79, p=0.005; Adj. RR=0.86, p=0.082, respectively). The percentages of mild obstructive abnormalities in the low, medium, and high initial dioxin categories were 32.5, 34.8, and 20.0, respectively. No significant difference was seen in the moderate versus no obstructive abnormalities contrast or the severe versus no obstructive abnormalities contrast (p>0.13 for all analyses).

The unadjusted Model 3 analysis revealed three significant or marginally significant differences between Ranch Hands and Comparisons in the percentage of participants with mild abnormalities. Ranch Hands in the background dioxin category had a higher percentage of mild obstructive abnormalities than did Comparisons (Table 18-12(e): 34.4% vs. 29.4%, Est. RR=1.26, p=0.071), as did Ranch Hands in the low dioxin category (Table 18-12(e): 35.7% vs. 29.4%, Est. RR=1.38, p=0.037). Ranch Hands in the high dioxin category had a lower percentage of mild obstructive abnormalities than did Comparisons (Table 18-12(e): 22.6% vs. 29.4%, Est. RR=0.70, p=0.031). A marginally significant greater percentage of Ranch Hands in the low dioxin category had a severe obstructive abnormality than did Comparisons (Table 18-12(e): 2.5% vs. 1.2%, Est. RR=2.37, p=0.080). After adjusting for covariates, only the difference in mild obstructive abnormalities between Ranch Hands in the high dioxin category and Comparisons remained marginally significant (Table 18-12(f): Adj. RR=0.74, p=0.096). No significant difference was detected in the moderate versus no obstructive abnormalities contrast (p>0.31 for all analyses).

The unadjusted Model 4 analysis showed a significant or marginally significant decreased risk of mild and severe obstructive abnormalities with increasing 1987 dioxin levels (Table 18-12(g): Est. RR=0.83, p<0.001, for the mild versus no obstructive abnormalities contrast; Est. RR=0.70, p=0.078, for the severe versus no obstructive abnormalities contrast). The percentages of mild obstructive abnormalities in the low, medium, and high 1987 dioxin categories were 33.7, 35.2, and 25.4, respectively. The percentages of severe obstructive abnormalities in the low, medium, and high 1987 dioxin categories were 2.1, 1.7, and 1.0, respectively. After adjusting for covariates, both contrasts became nonsignificant (p>0.17 for each contrast). No significant difference was observed in the moderate versus no obstructive abnormalities contrast (p>0.14 for all analyses).

18.2.3 Longitudinal Analysis

Longitudinal analyses were conducted on the ratio of observed FEV_1 to observed FVC to examine whether changes across time differed with respect to group membership (Model 1), initial dioxin (Model 2), and categorized dioxin (Model 3). Model 4 was not examined in longitudinal analyses because 1987 dioxin, the measure of exposure in these models, changes over time and was not available for all participants for 1982 or 1997. Summary statistics are provided for reference purposes for the 1987 and 1992 examinations. This measurement was not collected for the 1985 follow-up examination.

The longitudinal analysis for the ratio of observed FEV_1 to observed FVC examined the paired difference between the measurements from 1982 and 1997. These paired differences measured the change in the ratio over time. A logarithmic transformation was applied to 1.0 minus this ratio prior to calculating the paired differences for analytic purposes. Each of the three models used in the longitudinal analysis was adjusted for age and the ratio as measured in 1982 (see Chapter 7, Statistical Methods). The analyses of Models 2 and 3 also were adjusted for body fat at the time of the blood measurement of dioxin.

18.2.3.1 Laboratory Examination Variable

18.2.3.1.1 Ratio of Observed FEV_1 to Observed FVC

The Model 1 analysis of the change in the mean ratio of observed FEV_1 to observed FVC revealed a significant difference between Ranch Hands and Comparisons when combining all occupations (Table 18-13(a): difference=–0.005, p=0.048). The Ranch Hand group had a decrease in the mean ratio of 0.057 from 1982 to 1997, whereas the Comparison group showed a decrease of 0.052. Stratifying by occupation showed a marginally significant group difference among the enlisted flyers (difference=–0.014, p=0.072). The Ranch Hand enlisted flyers showed a decrease in the mean ratio of 0.072 between 1982 and 1997, compared to a decrease of 0.058 for the Comparison enlisted flyers.

The Model 2 analysis did not reveal a significant association between the change in the ratio of observed FEV_1 to observed FVC and initial dioxin (p=0.726).

The Model 3 analysis of the change in the ratio of observed FEV_1 to observed FVC revealed a marginally significant difference between the low and high dioxin categories combined and Comparisons (Table 18-13(c): difference=–0.004, p=0.052). The low and high dioxin categories combined had a decrease in the mean ratio of 0.056 between 1982 and 1997, versus a decrease of the mean ratio of 0.052 for the Comparison category.

Table 18-13. Longitudinal Analysis of the Ratio of Observed FEV_1 to Observed FVC

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Mean[a]/(n) Examination 1982	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	***Ranch Hand***	***0.817 (817)***	***0.818 (790)***	***0.764 (795)***	***0.760 (817)***	***–0.057***	***–0.005***	***0.048***
	Comparison	***0.816 (973)***	***0.818 (948)***	***0.765 (953)***	***0.764 (973)***	***–0.052***		
Officer	Ranch Hand	0.810 (311)	0.812 (304)	0.755 (306)	0.755 (311)	–0.055	–0.001	0.763
	Comparison	0.813 (380)	0.812 (368)	0.758 (375)	0.760 (380)	–0.054		
Enlisted Flyer	Ranch Hand	0.812 (148)	0.802 (142)	0.746 (145)	0.740 (148)	–0.072	–0.014	0.072
	Comparison	0.806 (143)	0.807 (141)	0.756 (141)	0.748 (143)	–0.058		
Enlisted Groundcrew	Ranch Hand	0.826 (358)	0.829 (344)	0.779 (344)	0.772 (358)	–0.054	–0.006	0.152
	Comparison	0.821 (450)	0.826 (439)	0.775 (437)	0.773 (450)	–0.048		

[a] Transformed from natural logarithm scale of (1 – ratio of observed FEV_1 to observed FVC).
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of natural logarithm of (1 – ratio of observed FEV_1 to observed FVC); results adjusted for natural logarithm of (1 – ratio of observed FEV_1 to observed FVC) in 1982 and age in 1997.

Note: Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

Table 18-13. Longitudinal Analysis of the Ratio of Observed FEV_1 to Observed FVC (Continued)

(b) MODEL 2: RANCH HANDS – INITIAL DIOXIN						
Initial Dioxin Category Summary Statistics					Analysis Results for Log_2 (Initial Dioxin)[b]	
	Mean[a]/(n) Examination					
Initial Dioxin	1982	1987	1992	1997	Adjusted Slope (Std. Error)	p-Value
Low	0.816 (154)	0.815 (153)	0.759 (149)	0.757 (154)	0.003 (0.009)	0.726
Medium	0.816 (158)	0.813 (155)	0.763 (155)	0.755 (158)		
High	0.835 (153)	0.842 (148)	0.792 (150)	0.785 (153)		

[a] Transformed from natural logarithm scale of (1 – ratio of observed FEV_1 to observed FVC).
[b] Results based on difference between natural logarithm of (1 – 1997 ratio of observed FEV_1 to observed FVC) and natural logarithm of (1 – 1982 ratio of observed FEV_1 to observed FVC) versus $\log_2$ (initial dioxin); results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of (1 – 1982 ratio of observed FEV_1 to observed FVC), and age in 1997; because of the transformation used, a negative slope implies a positive association between the ratio and $\log_2$ (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

Table 18-13. Longitudinal Analysis of the Ratio of Observed FEV_1 to Observed FVC (Continued)

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY							
Dioxin Category	Mean[a]/(n) Examination				Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
	1982	1987	1992	1997			
Comparison	0.816 (945)	0.818 (922)	0.765 (926)	0.763 (945)	–0.052		
Background RH	0.810 (346)	0.809 (329)	0.754 (336)	0.752 (346)	–0.059	–0.007	0.486
Low RH	0.819 (229)	0.816 (226)	0.763 (222)	0.758 (229)	–0.061	–0.009	0.109
High RH	0.826 (236)	0.831 (230)	0.780 (232)	0.774 (236)	–0.052	0.000	0.161
Low plus High RH	0.822 (465)	0.823 (456)	0.772 (454)	0.766 (465)	–0.056	–0.004	0.052

[a] Transformed from natural logarithm scale of (1 – ratio of observed FEV_1 to observed FVC).
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of natural logarithm of (1 – 1997 ratio of observed FEV_1 to observed FVC); results adjusted for percent body fat at the date of the blood measurement of dioxin, natural logarithm of (1 – 1982 ratio of observed FEV_1 to observed FVC), and age in 1997.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

18.3 DISCUSSION

Although the presence of pulmonary disease is often apparent based on the participant's history and physical examination, confirmation of the diagnosis and quantification of the degree of pulmonary impairment usually requires collection of the laboratory data analyzed in the current chapter. In addition, because the lung is often involved secondarily in numerous infectious, inflammatory, and neoplastic disorders, the assessment of lung disease should include the type of comprehensive multi-system review conducted in these examinations and reported in other chapters.

Historical information on the occurrence of pulmonary disease must be interpreted with caution in the absence of medical record verification. Many of the cardinal symptoms of lung disease, including dyspnea, chest pain, and exercise intolerance, are common to cardiovascular disease as well, particularly ischemic heart disease, and are misinterpreted frequently as to cause. Wheezing, assumed by the patient to be indicative of asthma, may in fact be reflective of hemodynamic compromise in congestive heart failure. "Pneumonia" and "pneumonitis" are often confused by patients in relating the medical history. Thus, all episodes of pulmonary disease were verified by medical records and only documented occurrences were analyzed.

The physical examination variables studied can provide valuable clues to the presence of pulmonary disease; however, in lacking specificity, these data have limitations in confirming a diagnosis. Wheezes and hyperresonance, for example, will occur in obstructive airway disease in asthma or in emphysema secondary to cigarette use. Dullness to percussion, a finding common to many disorders, will occur in consolidation from atelectasis, infections, pleural thickening, or pleural effusion.

In view of the limitations of the participant's history and physical examination noted above, added emphasis is placed on screening laboratory data in the diagnosis of respiratory disease. The chest x ray, when normal, is highly reliable in excluding pulmonary parenchymal disease, although several exceptions must be recognized. Solitary lesions less than 6 millimeters, miliary granulomatous infection, and early interstitial disease, among others, may be present but not detectable radiographically. Furthermore, it is recognized clinically that the chest x ray is not sensitive to the detection of obstructive airway disease in an early stage. On the other hand, the chest x ray may reveal an early occult malignancy in an asymptomatic patient and afford a rare opportunity for cure.

Spirometry has been used as a clinical tool to measure static lung volumes and to detect respiratory disease for more than a century. Dynamic indices, relating changes in lung volume to time, were first developed more than 50 years ago and, with computerization, have been refined to a high degree of accuracy and reproducibility. To be valid, spirometry requires that particular attention be paid to technician training and to eliciting the full cooperation of the patient. In spirometry, a premium is placed on using identical techniques in longitudinal studies. These factors received special emphasis in this study.

The spirometric indices evaluated in this section, FEV_1 and FVC, are designed to measure lung volume. Height is the principal determinant of static lung volume, as measured by the vital capacity, whereas dynamic flow measurements depend more on physical strength. Accordingly, all indices require correction for height and age. Race-specific variations in spirometric indices, reflective of differences in body habitus, have been well documented and recently summarized (44). Blacks, for example, have FVC and FEV_1 values that average 12 to 15 percent less than Caucasian Americans of comparable height.

In clinical practice, it is convenient to divide respiratory disease into two broad categories: "restrictive" and "obstructive." "Restrictive" disease is characterized by reduced vital capacity as seen in interstitial fibrosis or reduced lung volume consequent to surgical resection. In "obstructive" disease, whether associated with asthma or with cigarette use, the flow-dependent index, FEV_1, is abnormally prolonged.

The analyses of the dependent variable-covariate associations confirm observations that are well established in clinical practice. Lifetime cigarette smoking history was a consistent and highly significant risk factor for the development of bronchitis and, in a dose-response pattern, associated with abnormalities in all of the laboratory indices examined. At each of the AFHS examinations, all nicotine-dependent participants were counseled on smoking cessation. Of interest, over the 15-year course of these examinations, the percentage of nicotine-dependent participants has fallen from 42 percent in 1982 to just under 20 percent in 1997. With advancing age, an increase in respiratory disease was confirmed by history and on physical examination, as was a progressive age-related reduction in the dynamic index of pulmonary function, the FEV_1 and, to a lesser extent, the vital capacity. Because spirometric indices were not corrected for race in this follow-up examination, Blacks were found to have reductions of approximately 10 percent in FVC, FEV_1, and the ratio of observed FEV_1 to observed FVC. Finally, the analyses of body fat confirmed the well recognized reduction in vital capacity and its derived indices associated with obesity.

The analyses of historical variables yielded inconsistent results. Ranch Hands were more likely than Comparisons to have had bronchitis and asthma, whereas the prevalence of pneumonia was greater in Comparisons. In none of the contrasts were the differences significant. Similar to the 1992 examinations, but of unknown cause, Ranch Hand enlisted flyers appeared to be at selective risk relative to Comparisons with respect to the history of bronchitis (27.8% vs. 19.1%). Within this occupational stratum, there are no longer any significant group differences on physical examination or by chest x ray. Further, in none of these analyses was there any relation with the body burden of dioxin.

A significantly increased risk of mild obstructive abnormality was found in Ranch Hand officers. This finding was not present in 1992. The meaning of the finding is uncertain because the risk was not significantly increased in Ranch Hand enlisted groundcrew—the subgroup with the highest dioxin levels. The relation between mild obstructive abnormality in Ranch Hand officers and indicators of herbicide exposure, such as job (pilot, navigator, nonflyer), the number of missions flown, the percentage of missions that were herbicide missions, and reported drinking of herbicide (yes, no) will be summarized in a separate report.

In none of the static and dynamic spirometric indices were any significant group differences defined, nor was there evidence for any adverse effect associated with prior dioxin exposure.

Longitudinal analyses of the ratio of observed FEV_1 to observed FVC confirms the gradual decline in this index associated with age in both the Ranch Hand and Comparison cohorts. Similar to the 1992 results, in the enlisted flyer category, Ranch Hands had a slightly greater reduction in the ratio than did Comparisons, but the difference (–0.072 vs. –0.058) is not physiologically meaningful.

In conclusion, apart from the marginally significant increase in bronchitis in enlisted flyers noted above, the historical, physical examination, and laboratory data analyzed in the current section revealed no evidence for an increase in pulmonary disease in the Ranch Hand cohort relative to Comparisons. The results also confirmed numerous dependent variable-covariate associations documented in previous AFHS examinations.

18.4 SUMMARY

18.4.1 Model 1: Group Analysis

A marginally significant difference in bronchitis was observed between Ranch Hand and Comparison enlisted flyers in unadjusted and adjusted analyses. Ranch Hand enlisted flyers had a higher prevalence of bronchitis than did Comparison enlisted flyers. Ranch Hand officers had a significantly higher prevalence of mild obstructive abnormality than did Comparison officers in both unadjusted and adjusted analyses. All other tests of the association of group and the pulmonary variables were nonsignificant. The results of the group analyses are summarized in Table 18-14.

Table 18-14. Summary of Group Analysis (Model 1) for Pulmonary Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Medical Records				
Asthma (D)	NS	NS	ns	NS
Bronchitis (D)	NS	NS	NS*	NS
Pneumonia (D)	ns	ns	NS	ns
Physical Examination				
Thorax and Lung Abnormalities (D)	NS	NS	NS	ns
Laboratory				
X-ray Interpretation (D)	NS	NS	NS	NS
FVC (C)	NS	NS	NS	NS
FEV_1 (C)	ns	ns	ns	NS
Ratio of Observed FEV_1 to Observed FVC (C)[a]	ns	ns	ns	NS
Loss of Vital Capacity (D):				
Mild vs. None	ns	NS	ns	NS
Moderate or Severe vs. None	ns	NS	ns	ns
Obstructive Abnormality (D):				
Mild vs. None	NS	+0.034	ns	NS
Moderate vs. None	NS	NS	NS	ns
Severe vs. None	NS	NS	NS	ns

Note: NS or ns: Not significant ($p>0.10$).
NS*: Marginally significant ($0.05<p\leq0.10$).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00 for discrete analysis.
[a]Difference of means negative considered adverse for this variable.

P-value given if $p\leq0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Variable	ADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Medical Records				
Asthma (D)	NS	NS	ns	NS
Bronchitis (D)	NS	NS	NS*	NS
Pneumonia (D)	ns	ns	NS	ns
Physical Examination				
Thorax and Lung Abnormalities (D)	ns	NS	ns	ns
Laboratory				
X-ray Interpretation (D)	NS	NS	NS	NS
FVC (C)	NS	NS	NS	NS
FEV_1 (C)	NS	NS	ns	NS
Ratio of Observed FEV_1 to Observed FVC (C)[a]	ns	ns	ns	NS

Table 18-14. Summary of Group Analysis (Model 1) for Pulmonary Variables (Ranch Hands vs. Comparisons) (Continued)

Variable	ADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Loss of Vital Capacity (D):				
Mild vs. None	ns	NS	ns	NS
Moderate or Severe vs. None	ns	NS	ns	ns
Obstructive Abnormality (D):				
Mild vs. None	NS	+0.041	ns	ns
Moderate vs. None	ns	NS	NS	ns
Severe vs. None	NS	NS	NS	ns

Note: NS or ns: Not significant (p>0.10).
NS*: Marginally significant (0.05<p≤0.10).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00 for discrete analysis.
[a]Difference of means negative considered adverse for this variable.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

18.4.2 Model 2: Initial Dioxin Analysis

The results of the tests of association between the pulmonary variables and initial dioxin are summarized in Table 18-15. For the unadjusted analysis of pneumonia, a significant decrease in pneumonia was found as initial dioxin increased. After covariate adjustment, the association was no longer significant. The ratio of the observed FEV_1 to the observed FVC significantly increased as initial dioxin increased, but this association was also nonsignificant after adjustment for covariates. The prevalence of a mild obstructive abnormality significantly decreased as initial dioxin increased in the unadjusted analysis. This association was marginally significant after adjustment for covariates. All other tests of association with initial dioxin were nonsignificant.

Table 18-15. Summary of Initial Dioxin Analysis (Model 2) for Pulmonary Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Asthma (D)	NS	NS
Bronchitis (D)	NS	NS
Pneumonia (D)	ns*	ns
Physical Examination		
Thorax and Lung Abnormalities	NS	NS
Laboratory		
X-ray Interpretation (D)	ns	ns
FVC (C)	NS	ns
FEV_1 (C)	NS	NS

Table 18-15. Summary of Initial Dioxin Analyses (Model 2) for Pulmonary Variables (Ranch Hands Only) (Continued)

Variable	Unadjusted	Adjusted
Ratio of Observed FEV_1 to Observed FVC (C)[a]	–0.023	ns
Loss of Vital Capacity (D):		
Mild vs. None	ns	ns
Moderate or Severe vs. None	ns	NS
Obstructive Abnormality (D):		
Mild vs. None	–0.005	ns*
Moderate vs. None	ns	ns
Severe vs. None	ns	ns

Note: NS or ns: Not significant (p>0.10).
ns*: Marginally significant (0.05<p≤0.10).
C: Continuous analysis.
D: Discrete analysis.
–: Relative risk <1.00 for discrete analysis; slope negative for continuous analysis.
[a] Positive slope considered adverse for this variable; a negative slope implies an increase in the ratio because of the data transformation used.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or slope nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

18.4.3 Model 3: Categorized Dioxin Analysis

The results of the categorized dioxin analysis of the pulmonary variables are summarized in Table 18-16. Ranch Hands in the background dioxin category showed a marginally significant increase in bronchitis relative to Comparisons in the adjusted analysis. For the unadjusted and adjusted analyses of the x-ray interpretation, the background Ranch Hands exhibited a significantly higher percentage of abnormalities on the x ray than Comparisons. Unadjusted analyses revealed a higher prevalence of a mild obstructive abnormality for Ranch Hands in the background and low dioxin categories than for Comparisons. These differences between Ranch Hands and Comparisons became nonsignificant after adjustment for covariates. Ranch Hands in the high dioxin category had a significantly smaller prevalence of a mild obstructive abnormality than did Comparisons without adjustment for covariates. The prevalence was marginally significant after adjustment for covariates. Unadjusted analyses revealed a marginally higher prevalence of a severe obstructive abnormality between Ranch Hands in the low dioxin category and Comparisons. This difference between Ranch Hands and Comparisons became nonsignificant after adjustment for covariates.

Table 18-16. Summary of Categorized Dioxin Analysis (Model 3) for Pulmonary Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Medical Records				
Asthma (D)	NS	NS	NS	NS
Bronchitis (D)	NS	NS	NS	NS
Pneumonia (D)	ns	NS	ns	ns
Physical Examination				
Thorax and Lung Abnormalities (D)	ns	NS	NS	NS
Laboratory				
X-ray Interpretation (D)	+0.013	NS	ns	ns
FVC (C)	NS	ns	NS	ns
FEV_1 (C)	ns	ns	NS	ns
Ratio of Observed FEV_1 to Observed FVC (C)[a]	ns	ns	NS	NS
Loss of Vital Capacity (D):				
Mild vs. None	NS	ns	ns	ns
Moderate or Severe vs. None	NS	ns	ns	ns
Obstructive Abnormality (D):				
Mild vs. None	NS*	+0.037	–0.031	ns
Moderate vs. None	NS	NS	ns	ns
Severe vs. None	NS	NS*	ns	ns

Note: NS or ns: Not significant (p>0.10).
NS*: Marginally significant (0.05<p≤0.10).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00 for discrete analysis.
–: Relative risk < 1.00 for discrete analysis.
[a] Difference of means negative considered adverse for this variable.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Variable	ADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Medical Records				
Asthma (D)	NS	NS	NS	NS
Bronchitis (D)	NS*	ns	NS	NS
Pneumonia (D)	ns	ns	ns	ns
Physical Examination				
Thorax and Lung Abnormalities (D)	ns	NS	NS	NS
Laboratory				
X-ray Interpretation (D)	+0.004	NS	ns	ns

Table 18-16. Summary of Categorized Dioxin Analysis (Model 3) for Pulmonary Variables (Ranch Hands vs. Comparisons) (Continued)

Variable	ADJUSTED: Background Ranch Hands vs. Comparisons	ADJUSTED: Low Ranch Hands vs. Comparisons	ADJUSTED: High Ranch Hands vs. Comparisons	ADJUSTED: Low plus High Ranch Hands vs. Comparisons
FVC (C)	ns	NS	NS	NS
FEV_1 (C)	ns	NS	NS	NS
Ratio of Observed FEV_1 to Observed FVC (C)[a]	ns	NS	NS	NS
Loss of Vital Capacity (D):				
Mild vs. None	NS	ns	ns	ns
Moderate or Severe vs. None	NS	ns	ns	ns
Obstructive Abnormality (D):				
Mild vs. None	NS	NS	ns*	ns
Moderate vs. None	NS	ns	ns	ns
Severe vs. None	NS	NS	ns	ns

Note: NS or ns: Not significant (p>0.10).
NS* or ns*: Marginally significant (0.05<p≤0.10).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00 for discrete analysis.
[a] Difference of means negative considered adverse for this variable

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

18.4.4 Model 4: 1987 Dioxin Level Analysis

The adjusted analysis of thorax and lung abnormalities revealed a marginally significant association between the prevalence of abnormalities and 1987 dioxin. The prevalence of abnormalities increased as 1987 dioxin increased. The unadjusted and adjusted analyses of the x-ray interpretation each exhibited a significant decrease in the prevalence of an x ray with abnormalities with an increase in 1987 dioxin. The ratio of the observed FEV_1 to the observed FVC significantly increased as 1987 dioxin increased, but this association was nonsignificant after adjustment for covariates. The adjusted analysis for a mild loss of vital capacity revealed a significant decrease in the loss of vital capacity as 1987 dioxin increased. The prevalence of a mild obstructive abnormality significantly decreased as 1987 dioxin increased in the unadjusted analysis. This association was nonsignificant after adjustment for covariates. The prevalence of a severe obstructive abnormality showed a marginally significant decrease as 1987 dioxin increased, but this association was also nonsignificant after adjustment for covariates. The results for the variables described above, as well as the other pulmonary variables, are summarized in Table 18-17.

Table 18-17. Summary of 1987 Dioxin Analysis (Model 4) for Pulmonary Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Asthma (D)	NS	NS
Bronchitis (D)	ns	ns
Pneumonia (D)	ns	ns
Physical Examination		
Thorax and Lung Abnormalities (D)	NS	NS*
Laboratory		
X-ray Interpretation (D)	–0.015	–0.015
FVC (C)	ns	NS
FEV_1 (C)	NS	NS
Ratio of Observed FEV_1 to Observed FVC (C)[a]	–<0.001	ns
Loss of Vital Capacity (D):		
Mild vs. None	ns	–0.046
Moderate or Severe vs. None	ns	ns
Obstructive Abnormality (D):		
Mild vs. None	–<0.001	ns
Moderate vs. None	ns	ns
Severe vs. None	ns*	ns

Note: NS or ns: Not significant (p>0.10).
NS* or ns*: Marginally significant (0.05<p≤0.10).
C: Continuous analysis.
D: Discrete analysis.
–: Relative risk <1.00 for discrete analysis; slope negative for continuous analysis.
[a] Positive slope considered adverse for this variable; a negative slope implies an increase in the ratio because of the data transformation used.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or slope nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

18.5 CONCLUSION

To assess the pulmonary status for the 1997 AFHS follow-up examination, verified histories of asthma, bronchitis, and pneumonia were studied. A composite measure of thorax and lung abnormalities, as determined from the presence of asymmetrical expansion, hyperresonance, dullness, wheezes, rales, chronic obstructive pulmonary diseases, or the physician's assessment of abnormality, also was analyzed. A routine chest x ray and five measures of pulmonary function using standard spirometric techniques were analyzed.

Few significant increases in adverse pulmonary conditions were observed for Ranch Hands, and isolated and inconsistent associations between the pulmonary endpoints and increased dioxin were seen. No consistent pattern or dose-response relation was evident. Ranch Hands in the background dioxin category exhibited a significantly higher percentage of abnormalities on the chest x-ray than did Comparisons. Ranch Hand officers had a significantly higher prevalence of mild obstructive abnormality than did

Comparison officers; the corresponding contrast was not significant in 1992, and officers were not analyzed as a separate stratum in 1982, 1985, or 1987.

In summary, analysis of historical, physical examination, and laboratory data revealed no relation between dioxin levels and pulmonary disease; however, the prevalence of mild obstructive abnormalities was significantly increased in Ranch Hand officers. The meaning of this finding is unclear because the risk was not significantly increased in Ranch Hand enlisted groundcrew—the military occupation with the highest dioxin levels.

REFERENCES

1. Kayser, K., M. Schonberg, S. Tuengerthal, and I. Vogt-Moykopf. 1986. Chronic progressive diffuse alveolar damage probably related to exposure to herbicides. *Klin Wochenschr* 64:44-8.

2. Kancir, C. B., C. Andersen, and A. S. Olesen. 1988. Marked hypocalcemia in a fatal poisoning with chlorinated phenoxy acid derivatives. *Clinical Toxicology* 26:257-64.

3. Meulenbelt, J., J. H. Zwaveling, P. van Zoonen, and N. C. Notermans. 1988. Acute MCPP intoxication: Report of two cases. *Human Toxicology* 7:289-92.

4. Tuteja, N., F. J. Gonzalez, and D. W. Nebert. 1985. Developmental and tissue-specific differential regulation of the mouse dioxin-inducible P1-450 and P3-450 genes. *Developmental Biology* 112:177-84.

5. Kurl, R. N., K. C. Chaudhary, and C. A. Villee. 1986. Characterization and control of cytosolic binding proteins for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in the rat lung. *Pharmacology* 33:181-9.

6. Devereux, T. R., M. W. Anderson, and S. A. Belinsky. 1988. Factors regulating activation and DNA alkylation by 4-(N-methyl-N-nitrosamino)-1-(3-pyridyl)-1-butanone and nitrosodimethylamine in rat lung and isolated lung cells and the relationship to carcinogenicity. *Cancer Research* 48:4215-21.

7. Domain, B. A., T. R. Devereux, J. R. Fouts, and R. M. Philpot. 1986. Pulmonary cytochrome P-450 isozyme profiles and induction by 2,3,7,8-tetrachlorodibenzo-p-dioxin in Clara and type II cells and macrophages isolated from rabbit lung. *Federal Proceedings* 45:321.

8. Domain, B. A., and R. M. Philpot. 1986. The effect of substrate on the expression of activity catalyzed by cytochrome P-450 metabolism mediated by rabbit isozyme 6 in pulmonary microsomal and reconstituted monooxygenase systems. *Archives of Biochemistry and Biophysics* 246:128-42.

9. Domain, B. A., T. R. Devereux, and R. M. Philpot. 1986. The cytochrome P-450 monooxygenase system of rabbit lung enzyme components activities and induction in the nonciliated bronchiolar epithelial Clara cell alveolar type II cell and alveolar macrophage. *Molecular Pharmacology* 30:296-303.

10. Vanderslice, R. R., B. A. Comin, G. T. Carver, and R. M. Philpot. 1987. Species-dependent expression and induction of homologues of rabbit cytochrome P-450 isozyme 5 in liver and lung. *Molecular Pharmacology* 31:320-5.

11. Mathews, J. M., and J. R. Bend. 1986. N-alkylaminobenzotriazoles as isozyme-selective suicide inhibitors of rabbit pulmonary microsomal cytochrome P-450. *Molecular Pharmacology* 30:25-32.

12. Overby, L. H., S. Nishio, A. Weir, G. T. Carver, C. S. Plopper, and R. M. Philpot. 1992. Distribution of cytochrome P-450 1A1 and NADPH-cytochrome P-450 reductase in lungs of rabbits treated with 2,3,7,8-tetrachlorodibenzo-p-dioxin: ultrastructural immunolocalization in in-situ hybridization. *Molecular Pharmacology* 41:1039-46.

13. Roberts, E. A., C. L. Golas, and A. B. Okey. 1986. Ah receptor mediating induction of aryl hydrocarbon hydroxylase: Detection in human lung by binding of 2,3,7,8-[3H] tetrachlorodibenzo-p-dioxin. *Cancer Research* 46:3739-43.

14. Beebe, L. E., S. S. Park, and L. M. Anderson. 1990. Induction responses in mouse liver and lung following a single intraperitoneal dose of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Federation of American Societies for Experimental Biology Journal* 4:A345.

15. Nessel, C. S., M. A. Amoruso, T. H. Umbreit, R. J. Meeker, and M. A. Gallo. 1989. Induction of cytochrome P-450 as a marker of the transpulmonary absorption of TCDD. *Toxicologist* 9:120.

16. Nessel, C. S., M. A. Amoruso, T. H. Umbreit, and M. A. Gallo. 1990. Hepatic aryl hydrocarbon hydroxylase and cytochrome P450 induction following the transpulmonary absorption of TCDD from intratracheally instilled particles. *Fundamental and Applied Toxicology* 15:500-9.

17. Suskind, R. R., and V. H. Hertzberg. 1984. Human health effects of 2,4,5-T and its toxic contaminants. *Journal of the American Medical Association* 251:2372-80.

18. Calvert, G. M., M. H. Sweeney, J. A. Morris, M. A. Fingerhut, R. W. Hornung, and W. E. Halperin. 1991. Evaluation of chronic bronchitis, chronic obstructive pulmonary disease, and ventilatory function among workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *American Review of Respiratory Disease* 144(6):1302-6.

19. Kociba, R. J., D. G. Keyes, J. E. Beyer (reference 7, ch. 14), R.M. Carreon, C. E. Wade, D. A. Dittenber, R. P. Kalnins, L. E. Frauson, C. N. Park, S. D. Barnard, R. A. Hummel, and C. G. Humiston. 1978. Results of a two-year chronic toxicity and oncogenicity study of 2,3,7,8-tetrachlorodibenzo-p-dioxin in rats. *Toxicology and Applied Pharmacology* 46:279-303.

20. Van Miller, J. P., J. J. Lalich, and J. R. Allen. 1977. Increased incidence of neoplasms in rats exposed to low levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Chemosphere* 9:537-44.

21. NTP (National Toxicology Program). 1982. Carcinogenesis Bioassay of 2,3,7,8-tetrachlorodibenzo-p-dioxin (Case No. 1746-01-6) in Osborne-Mendel Rats & B6C3F1 Mice (Gavage Study). Tech. Rept. Series No. 209. National Toxicology Program, Research Triangle Park, NC. 195 pp.

22. Allen, J. R., D. A. Barsotti, J. P. Van Miller, L. J. Abrahamson, and J. J. Lalich. 1977. Morphological changes in monkeys consuming a diet containing low levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Food and Cosmetics Toxicology* 15:401-10.

23. Zober, A., P. Messerer, and P. Huber. 1990. Thirty-four-year mortality followup of BASF employees exposed to 2,3,7,8-TCDD after the 1953 accident. *International Archives of Occupational and Environmental Health* 62:139-57.

24. Zober, A., M. G. Ott, and P. Messerer. 1994. Morbidity followup study of BASF employees exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) after a 1953 chemical reactor incident. *Occupational and Environmental Medicine* 51:479-86.

25. Bertazzi, P. A., C. Zocchetti, A. C. Pesatori, S. Guercilena, M. Sanarico, and L. Radice. 1989. Mortality in an area contaminated by TCDD following an industrial incident. *Medicina del Lavoro* 80:316-29.

26. Bertazzi, P. 1991. Long-term effects of chemical disasters. Lessons and results from Seveso. *Science of the Total Environment* 106:5-20.

27. Bertazzi, P. A., C. Zocchetti, A. C. Pesatori, S. Guercilena, M. Sanarico, and L. Radice. 1989. Ten-year mortality study of the population involved in the Seveso incident in 1976. *American Journal of Epidemiology* 129:1187-200.

28. Wolfe, W. H., J. E. Michalek, J. C. Miner, A. Rahe, J. Silva, W. F. Thomas, W. D. Grubbs, M. B. Lustik, T. G. Karrison, R. H. Roegner, and D. E. Williams. 1990. Health status of Air Force veterans occupationally exposed to herbicides in Vietnam. I. Physical health. *Journal of the American Medical Association* 264:1824-31.

29. Roegner, R. H., W. D. Grubbs, M. B. Lustik, A. S. Brockman, S. C. Henderson, D. E. Williams, W. H. Wolfe, J. E. Michalek, and J. C. Miner. 1991. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides. Serum dioxin analysis of 1987 examination results. NTIS: AD A 237 516-24. United States Air Force School of Aerospace Medicine. Brooks Air Force Base, Texas.

30. Boyle, C., P. Decoufle, R. J. Delaney, F. DeStefano, M. L. Flock, M. I. Hunter, M. R. Joesoef, J. M. Karon, M. L. Kirk, P. M. Layde, D. L. McGee, L. A. Moyer, D. A. Pollock, P. Rhodes, M. J. Scally, and R. M. Worth. 1987. Postservice Mortality Among Vietnam Veterans. Atlanta: Centers for Disease Control. CEH 86-0076. 143 pp.

31. Fett, M. J., J. R. Nairn, D. M. Cobbin, and M. A. Adena. 1987. Mortality among Australian conscripts of the Vietnam conflict era. II. Causes of death. *American Journal of Epidemiology* 125:878-84.

32. Watanabe, K. K., H. K. Kang, and T. L. Thomas. 1991. Mortality among Vietnam veterans: with methodological considerations. *Journal of Occupational Medicine* 33:780-5.

33. Michalek, J. E., W. H. Wolfe, and J. C. Miner. 1990. Health status of Air Force veterans occupationally exposed to herbicides in Vietnam. *Journal of the American Medical Association* 264:1832-6.

34. United States Centers for Disease Control. 1988. Health status of Vietnam veterans. In Part 2, Physical health. The Centers for Disease Control Vietnam experience study. *Journal of the American Medical Association* 259:2708-14.

35. Thomas, T. L., and H. K. Kang. 1990. Mortality and morbidity among Army Chemical Corps Vietnam veterans: A preliminary report. *American Journal of Industrial Medicine* 18:665-73.

36. Fingerhut, M. A., W. E. Halperin, D. A. Marlow, L. A. Piacitelli, P. A. Honchar, M. H. Sweeney, A. L. Greife, P. A. Dill, K. Steenland, and A. J. Suruda. 1991. Cancer mortality in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *New England Journal of Medicine* 324:212-8.

37. Breslin, P., H. K. Kang, Y. Lee, V. Burt, and B. M. Shepard. 1988. Proportionate mortality study of US Army and US Marine Corps veterans of the Vietnam War. *Journal of Occupational Medicine* 30:412-9.

38. Bullman, T. A., H. K. Han, and K. K. Watanabe. 1990. Proportionate mortality among US Army Vietnam veterans who served in Military Region I. *American Journal of Epidemiology* 132:670-4.

39. Thomas, W. F., W. D. Grubbs, T. G. Karrison, M. B. Lustik, R. H. Roegner, D. E. Williams, W. H. Wolfe, J. E. Michalek, J. C. Miner, and R. W. Ogershok. 1990. An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: I. 1987 followup examination results, May 1987 to January 1990. NTIS: AD A 222 573. United States Air Force School of Aerospace Medicine, Human Systems Division (AFSC), Brooks Air Force Base, Texas.

40. Grubbs, W. D., W. H. Wolfe, J. E. Michalek, D. E. Williams, M. B. Lustik, A. S. Brockman, S. C. Henderson, F. R. Burnett, R. G. Land, D. J. Osborne, V. K. Rocconi, M. E. Schreiber, J. C. Miner, G. L. Henriksen, and J. A. Swaby. 1995. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final Report. 1992 Followup Examination Results. NTIS: AD A 304 306, 304 308-316. United States Air Force School of Aerospace Medicine, Brooks Air Force Base, Texas.

41. American Thoracic Society. 1991. Lung Function Testing: Selection of Reference Values and Interpretative Strategies. *American Review of Respiratory Disease* 144:1202-18.

42. Knapik, J. J., A. R. L. Burse, and J. A. Vogel. 1983. Height, weight, percent body fat, and indices of adiposity for young men and women entering the Army. *Aviation, Space, and Environmental Medicine* 54:223-31.

43. Michalek, J. E., J. L. Pirkle, S. P. Caudill, R. C. Tripathi, D. G. Patterson Jr., and L. L. Needham. 1996. Pharmacokinetics of TCDD in Veterans of Operation Ranch Hand: 10-year Followup. *Journal of Toxicology and Environmental Health* 47:209-20.

44. Hankinson, J. L., J. R. Odencrantz, and K. B. Fedan. 1999. Spirometric reference values from a sample of the general U.S. population. *Respiratory and Critical Care Medicine* 159:179-87.

Table of Contents

19 CONCLUSIONS

19.1 INTRODUCTION

This section summarizes the conclusions drawn from the statistical analyses of data from the 1997 follow-up examination of the Air Force Health Study (AFHS). The 1997 follow-up examination was an extension of the baseline, 1985, 1987, and 1992 follow-up examinations. Health endpoints measured at the 1997 examination were analyzed for associations with herbicide exposure and body burden of serum dioxin and were examined longitudinally in relation to data from previous AFHS examinations. A full explanation of the study design and methodology, terminology, and interpretive considerations is provided in Chapters 1 through 8 of this report.

19.2 STUDY PERFORMANCE ASPECTS

A total of 2,121 veterans participated in the 1997 follow-up examination. Of the 1,101 eligible Ranch Hands, 870 (79.0%) participated in the 1997 follow-up examination. Participation was voluntary and consent forms were signed by the participant at the examination site. A total of 839 of the 1,151 eligible Original Comparisons (72.9%) participated. Of the 768 Replacement Comparisons eligible for the 1997 follow-up examination, 412 (53.6%) chose to attend the examination. A total of 1,251 Comparisons attended the 1997 follow-up examination. Eighty-six percent (819 of 949) of living Ranch Hands and 87 percent of living Comparisons (976 of 1,116) who were fully compliant at the baseline examination returned for the 1997 follow-up examination.

Although more Comparisons than Ranch Hands refused to participate in the 1997 follow-up examination, there were no significant differences in the reasons for refusal among the two groups. Logistics and health reasons were the most common reasons for refusal, although approximately 25 percent of noncompliant veterans were deemed hostile and a reason for refusal was not determined. Approximately 91 percent of noncompliant Original Comparisons were either replaced or required no replacement (e.g., the Original Comparison was deceased and no Replacement Comparison had been contacted previously).

Ranch Hands reported fair or poor health more often than did Comparisons. This pattern of Ranch Hands reporting poorer health has been observed since the baseline examination. In both groups, veterans who refused were more likely to report fair or poor health than those who were fully compliant. Ranch Hands reported a slightly higher use of medications, but no difference was seen in reported work loss between Ranch Hands and Comparisons.

In summary, the results of these analyses suggested that Ranch Hands may be reporting poorer health than Comparisons and that these group differences are present for both fully compliant participants and refusals. This holds true even after accounting for rank and age differences. In addition, the difference in the percentage of fully compliant participants and refusals reporting fair or poor health was similar for Ranch Hands and Comparisons.

19.3 STATISTICAL MODELS

The analysis of the 1997 follow-up examination results used four statistical models to evaluate the relation between the health status of study participants and their dioxin exposure and serum dioxin levels.

The first model specified contrasts between Ranch Hands and Comparisons using group as a proxy for herbicide exposure and did not incorporate serum dioxin measurements. The remaining three models all incorporated serum dioxin measurements in either 1987 dioxin levels or an estimate of initial exposure based on a first-order extrapolation to the time of tour of duty in Southeast Asia (SEA). The four models are summarized as follows:

- Model 1: Ranch Hands versus Comparisons, for all military occupations (officer, enlisted flyer, enlisted groundcrew) combined and for each military occupation separately
- Model 2: Estimated initial serum dioxin levels using Ranch Hand participants with greater than 10 parts per trillion (ppt) of 1987 lipid-adjusted dioxin
- Model 3: Ranch Hands categorized according to serum dioxin levels versus Comparisons with 10 ppt of 1987 lipid-adjusted dioxin or less
- Model 4: 1987 lipid-adjusted serum dioxin using Ranch Hands only.

In Model 1, the use of group and occupation as a surrogate for herbicide exposure was less subject to the possible biases based on health conditions that may occur with variation in dioxin elimination rates. An implicit underlying assumption was that Ranch Hands were exposed and Comparisons were not exposed to herbicides. Model 2 was based on initial dioxin levels that were extrapolated from lipid-adjusted dioxin measurements above background levels (10 ppt), assuming first-order kinetics and a constant dioxin elimination rate. These lipid-adjusted dioxin measurements were collected primarily at the 1987 examination and supplemented with measurements from the 1992 or 1997 examination when a 1987 measurement was not available. Model 3 was less dependent on the accuracy of the initial dioxin estimation algorithm, but all Ranch Hands with high serum dioxin levels were treated alike without emphasizing the unusually large dioxin doses received by some Ranch Hands. Model 4 was based on lipid-adjusted dioxin measurements and assumed nothing about dioxin elimination other than that Ranch Hands were exposed in Vietnam and their body burdens have decreased over time in an unspecified manner. The extrapolated initial dose and lipid-adjusted dioxin measurements may not be accurate measures of exposure if elimination rates differed among individuals.

Statistical analyses often were applied to clinical endpoints in continuous form (i.e., original measurements) as well as in discrete form (i.e., measurements grouped into categories based on abnormal levels). Analyses also were performed to account for the effects that demographic and personal characteristics (covariates) may have had on the clinical measurements. Such analyses are termed "adjusted analyses." The relation between health and the measures of exposure in the four models described above are summarized in the next section. The relation between covariates and measures of herbicide or dioxin exposure are described in Chapter 8.

Throughout this report, dioxin levels were used as measures of both exposure to dioxin itself and exposure to dioxin-contaminated herbicides, including Herbicide Orange. Direct contrasts of Ranch Hand and Comparison veterans (Model 1) address the hypothesis of health effects attributable to any herbicide exposure experienced by Ranch Hand veterans during Operation Ranch Hand. Models involving dioxin levels address the hypothesis that health effects change with the amount of exposure. Dioxin levels were used as a measure of exposure to dioxin-contaminated herbicides because it was expected that as exposure to such herbicides increased, dioxin levels should increase. The dioxin levels, therefore, served as a direct biomarker of exposure to dioxin-contaminated herbicides. No other direct measure or estimate of herbicide exposure is available to address hypothetical dose-response relations

with health. Some indirect measures, such as self-report of skin contact among enlisted groundcrew, or simply being a Ranch Hand enlisted groundcrew member, are valuable alternatives because dioxin measures suggest that enlisted groundcrew experienced the heaviest exposures. Reported skin exposure was not addressed in this report, but enlisted groundcrew status was used in Model 1. The use of dioxin as a surrogate measure of exposure to dioxin-contaminated herbicides is consistent with the goal of the study, which is to determine whether health effects exist and can be attributed to occupational exposure to Herbicide Orange.

19.4 CLINICAL RESULTS

This section provides the conclusions from the analyses of the 10 clinical areas—general health, neoplasia, neurology, psychology, gastrointestinal, cardiovascular, hematology, endocrine, immunology, and pulmonary. Tables G-1 through G-24 of Appendix G present the results of the exposure analyses for each of the four models for 257 health endpoints analyzed in the 10 clinical chapters.

19.4.1 General Health Assessment

The self-perception of health analysis revealed significant differences between Ranch Hands and Comparisons, with more Ranch Hands than Comparisons indicating their health as fair or poor. As in previous examinations, the difference was most apparent in enlisted groundcrew, who had the highest average dioxin levels. This observation also was confirmed in the categorized dioxin analysis, where Ranch Hands with the highest dioxin levels perceived their health as fair or poor more often than Comparisons. Also, among Ranch Hands, those with the higher 1987 dioxin levels reported fair or poor health more often than Ranch Hands with lower levels. These results were consistent with the 1985, 1987, and 1992 examinations. No group differences were noted in the appearance of illness or relative age, as recorded by examining physicians, nor were these variables correlated with serum dioxin levels in the Ranch Hand cohort.

The analysis of body fat indicated positive associations with dioxin levels. The results of the 1997 examination confirmed those of the 1992 examination and appear consistent with a difference in dioxin pharmacokinetics in obese versus lean individuals.

No differences in the percentages of abnormal erythrocyte sedimentation rates between Ranch Hands and Comparisons or relations between abnormal erythrocyte sedimentation rates and dioxin levels were observed during the 1997 examination. Erythrocyte sedimentation rates increased as 1987 dioxin levels increased.

Longitudinal analyses showed that Ranch Hands, particularly the two enlisted strata, had a greater percentage of abnormal erythrocyte sedimentation rates than did Comparisons during the 15 years of the study since 1982. These analyses also showed that the percentages of abnormalities increased from 1982 to 1997 as dioxin levels increased. This result was seen at the 1987 study, but not in 1992. This positive association raises the possibility of a subtle inflammatory, infectious, or occult malignant disease process related to the body burden of dioxin.

In conclusion, fair or poor self-perception of health displayed an adverse association with dioxin, but the relation with other health conditions is unknown. Increased body fat was associated with increased levels of dioxin, a finding most likely related to the pharmacokinetics of dioxin. Longitudinal analyses indicated an increased risk of an abnormal erythrocyte sedimentation rate in Ranch Hands over Comparisons in the 15 years of the AFHS, and a relation between abnormal erythrocyte sedimentation

rates and levels of dioxin during these 15 years. Other measures of general health revealed no association with levels of dioxin.

19.4.2 Malignant Neoplastic Diseases

At the end of 15 years of surveillance, Ranch Hands as a group exhibited a nonsignificant increase in the risk of malignant neoplastic disease relative to Comparisons (relative risk=1.06, 95% confidence interval: [0.80,1.41]). Military occupation contrasts were inconsistent and, therefore, not supportive of an adverse effect of herbicide or dioxin exposure on the occurrence of malignancies. Ranch Hand enlisted groundcrew, the occupation with the highest dioxin levels and, presumably, the highest herbicide exposure, exhibited a decreased prevalence (relative risk=0.78, 95% confidence interval: [0.51,1.19]). Enlisted flyers (relative risk=1.63, 95% confidence interval: [0.91,2.92]) and officers (relative risk=1.14, 95% confidence interval: [0.79,1.65]), occupations with lower dioxin levels, exhibited nonsignificant increases in the prevalence of malignant disease. The risk of malignant disease was nonsignificantly increased among Ranch Hands having the highest dioxin levels (relative risk=1.01, 95% confidence interval: [0.66,1.57]). Longitudinal analyses found no significant group differences with regard to the risk of malignancy and no pattern suggestive of an adverse relation between herbicide or dioxin exposure and the occurrence of malignant neoplastic disease.

19.4.3 Neurological Assessment

Four neurological disorders and extensive physical examination data on cranial nerve function, peripheral nerve status, and central nervous system coordination processes were analyzed in the neurological assessment. Inflammatory diseases, as verified by a medical records review, were increased in Ranch Hands relative to Comparisons in terms of both a group designation and categorized dioxin levels. However, three of the seven Ranch Hand diseases were caused by bacterial infections, suggesting that this finding is unrelated to herbicide or dioxin exposure. Peripheral disorders, as verified by a medical records review, increased in Ranch Hands as levels of 1987 dioxin increased. Neck range of motion abnormalities were increased in Ranch Hands relative to Comparisons in terms of both a group designation and categorized dioxin levels. The increase in abnormalities for Ranch Hands relative to Comparisons was noted in enlisted flyers. An increase in the risk of an abnormal muscle status was observed in Ranch Hand enlisted groundcrew. A significant association between initial dioxin and abnormalities of both visual fields and the patellar reflex was observed. Indices of polyneuropathy showed an increase in the prevalence of abnormality in Ranch Hands relative to Comparisons, and a positive association with initial dioxin, categorized dioxin, and 1987 dioxin levels.

In summary, although a common etiology in these findings is not apparent, a statistically significant increase in neurological disease appears in Ranch Hands historically, on physical examination, and as reflected in several of the composite polyneuropathy indices. Further, the associations of neck range of motion with categorized dioxin and a history of peripheral disorders with 1987 dioxin provide evidence of an association of neurological disease with elevated dioxin levels. The results of the analysis of the polyneuropathy indices also provide support of a statistical association between elevated dioxin levels and neurological disease; however, the clinical importance of this finding is uncertain.

19.4.4 Psychological Assessment

Five psychological disorders, which were verified by a medical records review, and 12 measures from the Symptom Checklist-90-Revised (SCL-90-R) inventory were examined in the psychological assessment. The SCL-90-R consisted of nine primary symptom dimensions and three broad indices of psychological

distress. In enlisted groundcrew, a significantly greater percentage of Ranch Hands than Comparisons had a history of other neuroses. All other significant results from analyses of Ranch Hands versus Comparisons showed a greater percentage of Comparisons than Ranch Hands with high SCL-90-R scores.

Associations between initial dioxin and the psychological endpoints were either nonsignificant or revealed a significant decrease in high (adverse) SCL-90-R scores as initial dioxin increased.

Differences in the history of psychological disorders and the prevalence of high SCL-90-R scores were examined between Comparisons and Ranch Hands categorized by dioxin levels. Ranch Hands in the low dioxin category and the low plus high dioxin category displayed a significantly higher occurrence of other neuroses than did Comparisons.

The relation between the 1987 dioxin levels and the psychological endpoints was examined and all results were nonsignificant.

In summary, Ranch Hand veterans exhibited a significantly increased prevalence of other neuroses among enlisted groundcrew, the military occupation with the highest dioxin levels and, presumably, the greatest herbicide exposure. Consistent increases in the prevalence of other neuroses with dioxin levels were found. No consistent relation was found between any SCL-90-R score and any measure of herbicide or dioxin exposure. The relation between other neuroses and herbicide exposure and dioxin levels will be described in greater detail in a separate report.

19.4.5 Gastrointestinal Assessment

The gastrointestinal assessment was based on eight disorders as determined from a review and verification of each participant's medical records, a physical examination determination of hepatomegaly, and 29 laboratory measurements or indices. The laboratory parameters included measurements of hepatic enzyme activity, hepatobiliary function, lipid and carbohydrate indices, and a protein profile. In addition, the presence of hepatitis and fecal occult blood was investigated.

Analyses of Ranch Hands versus Comparisons showed higher mean levels of alkaline phosphatase, α-1-antitrypsin, and haptoglobin in Ranch Hands than in Comparisons. In addition, significantly more Ranch Hands than Comparisons had high haptoglobin levels. A review of medical records showed a positive association between initial dioxin and other liver disorders. The other liver disorders condition consisted primarily of nonspecific laboratory test elevations. A significant association between initial dioxin and high levels of aspartate aminotransferase (AST) also was revealed.

Analyses of categorized dioxin revealed a significantly higher percentage of other liver disorders among Ranch Hands in the high dioxin category than among Comparisons. Higher mean levels of gamma glutamyl transferase (GGT), triglycerides, and α-1-antitrypsin were observed in Ranch Hands in the high dioxin category than in Comparisons. Ranch Hands in the high dioxin category had a greater prevalence of abnormal AST, triglyceride, and prealbumin levels than did Comparisons.

Many significant associations between the laboratory examination variables and 1987 dioxin levels were observed. In both the continuous and discrete forms, the hepatic enzymes alanine aminotransferase (ALT), AST, and GGT revealed significant, positive associations with 1987 dioxin. In addition, significant positive associations between 1987 dioxin and the ratio of cholesterol to high-density lipoprotein (HDL), triglycerides, and creatine phosphokinase were present.

In summary, the analysis of the 1997 follow-up data reflected patterns that have been observed and documented in prior examinations. Isolated group differences exist, but 1987 dioxin levels are strongly related to hepatic enzymes such as AST, ALT, and GGT, and to lipid-related health indices such as cholesterol, HDL, and triglycerides. These results are consistent with a dose-response effect and may be related to unknown subclinical effects of dioxin. Although hepatic enzymes and lipid-related indices showed an association with dioxin, there was no evidence of an increase in overt liver disease.

19.4.6 Cardiovascular Assessment

Analyses revealed that Ranch Hands had a significantly higher percentage of participants with a history of heart disease (excluding essential hypertension) than Comparisons and, in particular, among enlisted flyers. However, the risk of disease was not significantly increased in Ranch Hand enlisted groundcrew—the military occupation with the highest dioxin levels. The association between heart disease and initial dioxin showed a negative dose-response trend, with heart disease decreasing as initial dioxin increased. Furthermore, Ranch Hands in the background and low dioxin categories had more heart disease than did Comparisons, but this increase was not seen in Ranch Hands in the high dioxin category. Increases in tachycardia and other electrocardiograph (ECG) findings, such as pre-excitation, were seen for Ranch Hands in the high dioxin category, although the analyses were based on a small number of abnormalities. A significant positive association between initial dioxin and evidence of prior myocardial infarction from the ECG was observed in Ranch Hands, and a marginally significant positive association was observed between 1987 dioxin and evidence of prior myocardial infarction from the ECG. A positive association between 1987 dioxin and a history of essential hypertension also was observed in Ranch Hands. In contrast to previous AFHS examinations, no relation was found between peripheral pulse abnormalities and any measure of exposure.

In summary, in contrast to prior examinations, the current study has documented that Ranch Hands are more likely than Comparisons to have historical evidence for heart disease (excluding essential hypertension), but are no longer at greater risk for the occurrence of pulse deficits. By all other indices, the prevalence of cardiovascular disease appears similar in both cohorts. For the first time, there is evidence that levels of dioxin may be a risk factor for the development of essential hypertension and prior myocardial infarction as indicated by interpretation of the ECG. As of 1997, the verified history of essential hypertension was associated with 1987 dioxin, and the evidence of prior myocardial infarction from the ECG was associated with initial dioxin. These findings, in conjunction with the increase in the number of deaths caused by diseases of the circulatory system for Ranch Hand nonflying enlisted personnel based on the 1994 AFHS mortality update, showed associations that require further study. A biological mechanism for the relation among dioxin levels and heart disease is unknown.

19.4.7 Hematologic Assessment

Five cell count measures, six measures of absolute blood counts, a coagulation measure, and red blood cell morphology were analyzed. In the analyses of these variables, only platelet count exhibited significant dose-response associations with the levels of dioxin. Among enlisted personnel, Ranch Hands exhibited significantly higher mean platelet counts than did Comparisons. Ranch Hands in the high dioxin category also exhibited a significantly higher mean platelet count than did Comparisons. The mean differences were small and, therefore, the clinical importance of these findings is unknown. The results in the 1997 follow-up study parallel the findings of the 1987 and 1992 follow-up studies. In conclusion, apart from platelet count, there appears to be little evidence to support a relation between prior dioxin exposure and hematopoietic toxicity.

19.4.8 Endocrine Assessment

The assessment of the endocrine system yielded an extensive evaluation of thyroid, pancreatic, and gonadal function and their relation to dioxin exposure. A significantly increased risk of abnormally high thyroid stimulating hormone values was found in Ranch Hand enlisted groundcrew.

A positive association between diabetes and initial and 1987 dioxin was observed. Consistent with previous reports, the prevalence of diabetes among Ranch Hands with high dioxin levels was increased. A greater percentage of Ranch Hands than Comparisons used insulin to control their type 2 diabetes, primarily among officers and enlisted groundcrew. The percentage of Ranch Hands requiring insulin to control their type 2 diabetes increased with initial dioxin. A greater percentage of Ranch Hands in the high dioxin category required insulin to control their type 2 diabetes than did Comparisons. The percentage of Ranch Hands who treated their diabetes through diet only and the percentage who used oral hypoglycemics increased with 1987 dioxin level.

The time to diabetes onset was significantly shorter for Ranch Hands with higher initial dioxin and 1987 levels. Both fasting glucose and α-1-C hemoglobin increased in Ranch Hands as initial dioxin and 1987 dioxin increased. Increased α-1-C hemoglobin levels also were observed for Ranch Hands with high dioxin levels. The presence of fasting urinary glucose also increased with 1987 dioxin.

Although cause and effect have not been established, the results cited above provide further evidence for an association between diabetes and levels of dioxin.

19.4.9 Immunologic Assessment

The immunologic assessment was based on laboratory data on six lymphocyte cell surface markers, absolute lymphocyte counts, three quantitative immunoglobulins, and six measurements from an autoantibody panel. The six cell marker measurements were carried out on a random sample of approximately 40 percent of the participants because of the complexity of the assay and the expense of the tests.

Group analyses revealed significant findings for the analyses of CD16+56+ cell (natural killer cell) counts and for the mouse stomach kidney (MSK) smooth muscle antibody test in enlisted flyers. Among enlisted flyers, the mean CD16+56+ cell count was greater for Comparisons than for Ranch Hands, and a greater percentage of Comparisons than Ranch Hands had a smooth muscle antibody present. Negative smooth muscle antibody tests are considered to be normal. For these analyses, the magnitude of the mean differences was small and, therefore, the clinical importance of these findings is unknown.

Consistent with the previous two physical examinations, IgA increased significantly with initial dioxin, but was not significantly increased in enlisted groundcrew or the high dioxin category, and IgA did not increase significantly with 1987 dioxin. The IgA results, although significant, were small in magnitude and their clinical importance is unknown.

When comparing categorized dioxin levels between Ranch Hands and Comparisons, a significantly higher CD16+56+ cell count mean was observed among Comparisons than among Ranch Hands in the high dioxin category. Analyses revealed significant associations between 1987 dioxin levels and CD3+ cell (T cell) count, CD4+ cell (helper T cell) count, and CD3+CD4+ cell (helper T cell) count. The cell counts increased as 1987 dioxin increased.

In summary, these findings and the findings from past examinations do not provide evidence of a biologically meaningful dose-response effect for body burden of dioxin on parameters of immunologic assessment. The statistically significant relations suggest the need for continued evaluation.

19.4.10 Pulmonary Assessment

To assess pulmonary status, verified histories of asthma, bronchitis, and pneumonia were studied. A composite measure of thorax and lung abnormalities, as determined from the presence of asymmetrical expansion, hyperresonance, dullness, wheezes, rales, chronic obstructive pulmonary diseases, or the physician's assessment of abnormality, also was analyzed. A routine chest x ray and five measures of pulmonary function using standard spirometric techniques were analyzed.

Few significant increases in adverse pulmonary conditions were observed for Ranch Hands, and isolated and inconsistent associations between the pulmonary endpoints and dioxin were seen. No consistent pattern or dose-response relation was evident. Ranch Hands in the background dioxin category exhibited a significantly higher percentage of abnormalities on the chest x ray than did Comparisons. Ranch Hand officers had a significantly higher prevalence of mild obstructive abnormality than did Comparison officers; the corresponding contrast was not significant in 1992, and officers were not analyzed as a separate stratum in 1982, 1985, or 1987. The relation between mild obstructive abnormality in Ranch Hand officers and other indicators of herbicide exposure, such as job (pilot, navigator, nonflyer), the number of missions flown, the percentage of missions that were herbicide missions, and reported drinking of herbicide (yes, no) will be summarized in a separate report.

In summary, analysis of historical, physical examination, and laboratory data revealed no consistent relation between herbicide exposure or dioxin levels and pulmonary disease. The prevalence of mild obstructive abnormalities was significantly increased in Ranch Hand officers. The meaning of this finding is unclear because the risk was not significantly increased in Ranch Hand enlisted groundcrew—the military occupation with the highest dioxin levels.

19.5 INTERPRETIVE CONSIDERATIONS

Certain facts should be considered when drawing conclusions from the statistical analysis of the 1997 follow-up examination results. For example, there are often difficulties associated with multiple testing. With repeated statistical testing, the likelihood of a test indicating some artifactual association is high. But longitudinal comparisons of previous examinations may show a consistent association, supporting a non-artifactual relation. Longitudinal tests, however, of the same population clearly are not independent tests. If a chance association was present at the first physical examination, it would tend to persist in subsequent examinations. Conversely, depending on site and mode of action, the association would be expected to increase with time (if latency or other chronic effects predominate) or decrease with time (if the current dioxin level predominates in the mechanism). It is also important to note that some conditions do not appear with reasonable frequency until middle age or later. Therefore, in the early years of the study, an increased relative risk might have been masked by abnormalities too sparse for meaningful analysis.

The site and mode of action of dioxin in the body could itself either cause or obscure a relation. Receptors might be activated only after a certain dioxin threshold value had been exceeded—that is, a value exceeding the body's capability to safely store dioxin. If, on the other hand, dioxin caused a competitive inhibition of receptor actions normally stimulated by other substances, there might be a "no-threshold" effect. Depending on the nature (lipid or non-lipid) and type of function of the

hypothetical receptor site, an increase in body fat over time might either cause an increase in dioxin effect because of a greater volume of distribution or a decrease in dioxin effect because of a lesser concentration at the receptor site.

Statistical power is also an issue in a study of a population this size. A study with a population of 2,121 lacks power to determine increases in relative risks for rare events (such as soft tissue sarcoma) because such events are unlikely to occur in large numbers in a group this small. While certain occupational toxins have a clear diagnostic pathology (e.g., mesothelioma for asbestos, hepatic angiosarcoma for vinyl chloride) virtually nonexistent in the absence of the toxin, other toxins merely increase the risk of nondiagnostic pathology. For example, this study would likely not discern an increase in the relative risk for a rare tumor that does not have a clear diagnostic pathology. By assessing the pathology observed in association with other known environmental risk factors (e.g., tobacco use, alcohol use) it is sometimes possible to provide a limit in the magnitude of effect missed; however, this study has inherent bounds in detecting modest increases in relative risk for infrequent pathology.

A final difficulty is the presence of a true association that is noncausal. An example might be a condition not caused by dioxin, but resulting in or from an altered dioxin half-life. In this case, a correlation might be high in the total absence of causality.

Clearly, there are many issues to be considered in interpreting these results. With these issues in mind, certain assessments were made by looking at a number of factors. Among these factors are longitudinal trends, biological plausibility, consistency with animal toxicology, the presence of a dose-response relation, and strength of association. But, meeting all of these criteria would not guarantee causality, nor would failing these criteria guarantee the lack of an effect. It can be argued, however, that the good faith application of these particular methods should be the starting point for generating hypotheses for experimental examination through in vitro and in vivo testing, as well as through further epidemiological analysis of these and other dioxin-exposed groups.

19.6 SUMMARY

Based on the findings of the 1997 examination, and subject to the qualifications considered above, the study investigators have drawn the following conclusions.

19.6.1 Diabetes

Consistent with previously reported results, current data indicate a significant and potentially meaningful adverse relation between serum dioxin levels and diabetes. A significant dose-response was found, with Ranch Hands in the high dioxin category exhibiting an increase in disease prevalence (relative risk=1.47, 95% confidence interval: [1.00,2.17]). The finding is supported by a dioxin-related increase in disease severity, a decrease in the time from exposure to first diagnosis, and an increase in fasting glucose and α-1-C hemoglobin. Similar patterns were observed in 1987 and 1992.

19.6.2 Cardiovascular Abnormalities

Cardiovascular findings are mixed, but, in context with the increased cardiovascular mortality in nonflying enlisted Ranch Hands, are suggestive of an adverse effect of herbicide and dioxin exposure. As a group, Ranch Hands have experienced a statistically significant increase in the prevalence of heart disease (excluding essential hypertension) (relative risk=1.26, 95% confidence interval: [1.05,1.51]). The increase was more than doubled among enlisted flyers (relative risk=2.10, 95% confidence interval:

[1.27,3.28]) but not significantly increased among enlisted groundcrew (relative risk=1.10, 95% confidence interval: [0.84,1.42])—the military occupation with the highest dioxin levels. The prevalence of diagnosed essential hypertension and the percentage of Ranch Hands with ECG findings of prior myocardial infarction increased significantly with initial dioxin. Peripheral pulse abnormalities increased with dioxin levels in 1987 and 1992, but did not increase with dioxin levels in 1997. These findings, together with increased cardiovascular mortality in Ranch Hand nonflying enlisted personnel, suggest that herbicide or dioxin exposure may be related to cardiovascular abnormalities.

19.6.3 Peripheral Polyneuropathy

Although a common etiology is not apparent, a statistically significant increase in neurological disease appears in Ranch Hands historically, on physical examination, and as reflected in several of the composite polyneuropathy indices. Peripheral disorders, as verified by a medical records review, increased in Ranch Hands as levels of 1987 dioxin increased. Indices of bilateral peripheral polyneuropathy, confirmed by vibrotactile measurements in the feet, were significantly increased with initial dioxin level, significantly increased in the high dioxin category, and significantly increased with 1987 dioxin. These findings are new and appear consistent with polyneuropathies observed in studies of industrial exposure; however, the numbers of affected veterans are small and the clinical importance of the finding is uncertain.

19.6.4 Serum Lipid Abnormalities

There were consistent and significant increases in cholesterol, triglycerides, and the cholesterol-HDL ratio with initial and 1987 dioxin. HDL decreased significantly as dioxin increased. These findings also were observed in 1987 and 1992.

19.6.5 Liver Enzymes

Analysis of liver function reflected patterns that have been observed in prior examinations. Isolated group differences existed, but 1987 dioxin levels were strongly related to increases in hepatic enzymes, such as AST, ALT, and GGT and, as previously noted, cholesterol, triglycerides, and HDL. These results were consistent with an adverse dose-response and may be related to subclinical effects of unknown importance. Although hepatic enzymes increased with dioxin, there is no evidence of a corresponding increase in overt liver disease.

19.6.6 Malignant Neoplastic Disease

At the end of 15 years of surveillance, Ranch Hands as a group exhibited a nonsignificant increase in the risk of malignant neoplastic disease relative to Comparisons (relative risk=1.06, 95% confidence interval: [0.80,1.41]). Military occupation contrasts were inconsistent and, therefore, not supportive of an adverse effect of herbicide or dioxin exposure on the occurrence of malignancies. Ranch Hand enlisted groundcrew, the occupation with the highest dioxin levels and, presumably, the highest herbicide exposure, exhibited a decreased prevalence (relative risk=0.78, 95% confidence interval: [0.51,1.19]). Enlisted flyers (relative risk=1.63, 95% confidence interval: [0.91,2.92]) and officers (relative risk=1.14, 95% confidence interval: [0.79,1.65]), occupations with lower dioxin levels, exhibited nonsignificant increases in the prevalence of malignant disease. The risk of malignant disease was nonsignificantly increased among Ranch Hands having the highest dioxin levels (relative risk=1.01, 95% confidence interval: [0.66,1.57]). Longitudinal analyses found no significant group differences with regard to the

risk of malignancy and no pattern suggestive of an adverse relation between herbicide or dioxin exposure and the occurrence of malignant neoplastic disease.

19.7 CONCLUSION

In conclusion, diabetes and cardiovascular abnormalities represent the most important dioxin-related health problems seen in the AFHS. These two areas appear to have the greatest magnitude of effect in terms of quality of life and healthcare costs. Clearly, there are biological interrelations among both of these outcomes that make interpretations difficult. From a public health perspective, these two areas demand the greatest attention.

20 FUTURE DIRECTIONS

A careful review of the results of the last five physical examinations provides an opportunity to refine and focus the remaining examination of the Air Force Health Study. The current and prior examination outcomes have identified several medical tests requiring more intense evaluation and other analyses that can be reduced or eliminated in the 2002 study while still satisfying the study protocol.

The recently completed pharmacokinetic study of dioxin elimination in Ranch Hand veterans suggests that additional measurements per subject will not increase the precision of the estimated elimination rate. Thus, only those participants new to the study or those who have not already had a dioxin measurement will be invited to give blood for a dioxin assay in 2002.

In the final morbidity report, the Air Force intends to present a review of all herbicides sprayed by Operation Ranch Hand: 2,4-D, 2,4,5-T, picloram, and cacodylic acid, as well as 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD, or dioxin).

The Jenkins Activity Survey, used to determine personality type (a covariate in the analysis of cardiovascular data), has become inappropriate to administer to elderly retired men because the survey questions refer to on-the-job situations. Alternative measures of personality type will be sought as a replacement for this instrument. In this regard, a thorough reassessment of covariate adjustments across all clinical areas will be made. New covariates may be added and out-of-date covariates may be dropped.

A new series of statistical analyses, accounting for disease outcomes that may cross two or more clinical areas, will be considered. The possibility of second-order effects will be studied for inclusion in the next report. A multifactor approach may be used to assess psychological outcomes, for example. Changes to or replacement of the current longitudinal analyses will be considered to explicitly account for loss-to-follow-up and time-dependent covariates.

Statistical modeling will be reviewed. In particular, Model 2 will be reassessed to address possible changes in the elimination rate with body fat. An analysis stratified by category of body fat measured in an earlier examination may be used. Interactions between extrapolated initial dose, disease outcome, and percent body fat will be considered as alternate approaches.

Special efforts will be made to address loss-to-follow-up and possible differential compliance due to ill health or other reasons that would bias the study. Expanded questionnaires may be administered to noncompliant veterans and consideration will be given to sending medical teams to the homes of veterans who report that they are too ill to attend the physical examination.

Analyses of disease prevalence among all study subjects, regardless of their compliance to the 2002 physical examination, will be accomplished and summarized in the final report.

AIR FORCE HEALTH STUDY

FINAL REPORT

An Epidemiologic Investigation of
Health Effects in Air Force Personnel
Following Exposure to Herbicides

VOLUME III

1997 Follow-up Examination Results
May 1997 to February 2000

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United States Air Force

by

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in conjunction with

Scripps Clinic and National Opinion Research Center

22 February 2000

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AIR FORCE HEALTH STUDY

An Epidemiologic Investigation of
Health Effects in Air Force Personnel
Following Exposure to Herbicides

22 February 2000

Volume III

1997 Follow-up Examination Results

Human Effectiveness Directorate
Air Force Research Laboratory
Directed Energy Bioeffects Division
Population Research
311th Human Systems Wing (AFMC)
Brooks Air Force Base, Texas 78235

APPENDICES

TABLE OF CONTENTS-REPORT

APPENDIX A

Appendix A. Policies And Procedures for Dioxin Blood Collection and Processing

This appendix contains the following Scripps Clinic Policies and Procedures documents:

1. Dioxin Blood Collection
2. Dioxin Blood Processing
3. Dioxin Mailouts.

POLICIES AND PROCEDURES

Scripps Clinic
Department of Pathology
10666 N. Torrey Pines Road
La Jolla CA 92037

LABORATORY SECTION: **PHLEBOTOMY**
TITLE: **AFHS - DIOXIN BLOOD COLLECTION**
P.P. NUMBER: ISSUE DATE: 3/92 REVISION DATE:

1.0 PURPOSE

1.1 To collect blood sample for dioxin testing in accordance with Center for Disease Control standards.

2.0 SCOPE

2.1 Applies to designated Air Force Health Study participants.

3.0 MATERIALS

3.1 Blood - pack unit without anticoagulant - 600ml.
3.2 Alcohol swabs
3.3 PDI duo swabs
3.4 Sterile gauze
3.5 Adhesive tape
3.6 Gloves
3.7 Coban
3.8 Unit holders

4.0 PROCEDURE

4.1 On day 2, blood is drawn from designated participants with a 15 gauge needle into a blood pack unit without anticoagulant.
4.1.1 Blood pack units have been previously tested by the CDC for dioxin contamination.
4.2 Participants will have 280ml of blood drawn.
4.3 Select site for venipuncture.
4.3.1 On patients who have not yet had their physical exam, the dominant arm is preferred.

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4.4 Prepare site for venipuncture in the following manner:
  4.4.1 Ask participant if they are allergic to iodine.
    4.4.1.1 If allergic to iodine, use alcohol prep (70% isopropyl alcohol)
  4.4.2 Wash hands.
  4.4.3 Apply gloves.
  4.4.4 Scrub venipuncture site with Povidine-Iodine Scrub[tm] moving outward in a concentric spiral for at least 30 seconds to clean away fat, oils, dirt, etc.
  4.4.5 Remove scrub prep in a concentric spiral with sterile gauze and allow to dry.
  4.4.6 Apply tincture of iodine (Povidine-Iodine Scrub[tm]) in a circular fashion, starting at the proposed needle site, working outward. Allow to dry. (If allergic to iodine, use alcohol prep [70% isopropyl alcohol]).
  4.4.7 If not ready to do venipuncture immediately, cover site with dry sterile gauze.
4.5 Perform venipuncture and securely tape needle and tubing to arm.
4.6 Blood is collected into unit bag.
  4.6.1 Amount of blood is determined by weighing sample.
    4.6.1.1 When using Terumo scale, set scale at "0", fill bag to 280 ml.
    4.6.1.2 When using balance scale, set balance to 381gms.
    4.6.1.3 When amount needed is reached, release tourniquet, and clamp tubing with hemostat.
4.7 Remove needle from vein.
4.8 Have patient apply pressure to site for several minutes.
4.9 Apply pressure bandage to site using gauze and coban.
  4.9.1 Instruct patient not to remove bandage for at least 30-45 minutes.
4.10 Clamp tubing twice with hand sealer and clips.
  4.10.1 Cut tubing above clips.
  4.10.2 Dispose of needle in needle container.
4.11 Label unit bag with pre-printed label.
4.12 Place unit bag upright in vertical holder.
  4.12.1 Vertical unit holders are numbered according to order drawn.
  4.12.2 Units are placed in holders according to order of draw.
  4.12.3 Units are to remain upright at room temperature and allowed to clot for at least 7 hours.

5.0 SHORT DRAWS

5.1 In the event of a short draw, unit pack is to be weighed and the amount of blood noted on the unit label. "Short draw" should also be written on label in large letters.

6.0 MULTIPLE VENIPUNCTURES

6.1 If unable to collect sample with one venipuncture, ask patient if he is willing to be drawn again. If patient is willing, start procedure from beginning.
6.2 If patient is unwilling to be redrawn, notify nurse coordinator and Air Force monitor.
  6.2.1 Save labels and have test credited.

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POLICIES AND PROCEDURES

Scripps Clinic
Department of Pathology
10666 N. Torrey Pines Road
La Jolla CA 92037

LABORATORY SECTION: **SPECIMEN PROCESSING**
TITLE: **AIR FORCE HEALTH STUDY - DIOXIN BLOOD PROCESSING**
P.P. NUMBER: ISSUE DATE: 2/92 REVISION DATE: 2/97

1.0 PURPOSE: To process blood samples for dioxin testing using Center for Disease Control Standards as a guideline.

2.0 SCOPE: Applies to Clinical Pathology Medical Technicians involved in processing dioxin samples.

3.0 MATERIALS

- 3.1 Transfer pack units - 300 ml
- 3.2 Plasma transfer set
- 3.3 Plasma extractor
- 3.4 Vertical unit holders
- 3.5 Vertical unit holder boxes
- 3.6 Teflon lined lids
- 3.7 Teflon stoppers
- 3.8 Aluminum sealing caps
- 3.9 Aluminum cap sealer
- 3.10 Centrifuge bags
- 3.11 Handsealer/stripper
- 3.12 Shipping List
- 3.13 Wheaton bottles
  - 3.13.1 5 ml, 10 ml, 120 ml
- 3.14 Styrofoam mailing boxes
- 3.15 Dry ice

4.0 PROCEDURE

- 4.1 On the specific day the blood is drawn for dioxins, the units will be brought from the blood drawing station to specimen processing and allowed to clot, upright in their unit holders, at room temperature for a total of 7 hours.
- 4.2 Shipping list

C. Wiesner 2/18/97
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S. Buckner MT) 2/17/97

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4.2.1 The shipping list is a modified version of the list provided by the CDC.

4.2.2 Shipping list is prepared as follows: write participants name, ID number, Accession number, age, and check bottle sent.

4.2.3 Specify any deviations from collection, storage and shipment protocols, and date of occurrence.

4.3 Centrifuge of unit bags

4.3.1 Set temperature on floor model blood bank centrifuge between 4-10°C.

4.3.2 Unit bags are centrifuged in the order they are drawn.

4.3.3 The units of blood are placed inside plastic centrifuge bags.

4.3.3.1 The centrifuge bags are then balanced on the blood bank balance. No more than 3 units per centrifuge bag should be used.

4.3.3.2 If one centrifuge bag is heavier than the other, place small rubber stoppers into the centrifuge cups until units are balanced.

4.3.4 Centrifuge bags are placed into the centrifuge caps and spun for 15 minutes at 4500 RPMs.

4.3.5 Balance next group of unit bags for centrifuging.

4.4 Transfer of serum from unit bags to transfer packs.

4.4.1 Label transfer packs with patients aliquot label.

4.4.2 Labeled transfer packs are placed in vertical unit holders in the sequence they are to be transferred.

4.4.3 Serum is transferred from the spun unit bag to the transfer pack by plasmas extractor.

4.4.3.1 Place the unit bag on the plasma extractor with side not containing manufacturers label toward you.

4.4.3.2 Remove coupler cover of transfer pack unit.

4.4.3.3 Expose outlet port of blood pack unit.

4.4.3.4 Insert coupler into outlet port.

4.4.3.5 Release handle of plasma extractor and express the serum into the transfer pack. Do not allow red cells to enter the transfer pack. It is important to transfer the predominant amount of serum while preventing red cell contamination.

4.4.3.6 When the desired amount of serum is transferred, release the plasma extractor and clamp the tubing between the blood bag and the transfer pack using a hemostat clamp.

4.4.3.7 Seal the transfer tubing in 2 spots 1 inch apart using the Fenwal Hematron electronic sealer and severe tubing between seals

4.4.4 Transfer packs containing serum and any unit bags that need to be respun are placed in unsequential vertical unit holders and placed in vertical holder boxes.

4.4.5 Spinning of transfer packs

4.4.5.1 No more than 4 units (transfer packs) per centrifuge bag are to be balances at one time. In a 6 cup centrifuge this allows for 24 units of transferred serum to be spun at one time.

4.4.5.2 Transfer packs are to be spun at 4-10°C for 15 minutes at 4500 RPM in the floor model blood bank centrifuge.

4.5 Transfer of serum from transfer packs to Wheaton bottles

4.5.1 Wheaton bottles are labeled with patient aliquot labels

4 oz Wheaton bottle	S1 Serum dioxin
5 ml Wheaton bottle	S3 Lipid profile
10 ml Wheaton bottle	S4 Serum reserve

4 oz Wheaton bottle S1 Serum dioxin
(glass jar with screw cap)
5 ml Wheaton bottle S3 Lipid profile
10 ml Wheaton bottle S4 Serum reserve
4 oz Wheaton bottle S2 Serum dioxin *Save the S2 label and do not put on bottle. This label will only be used if the amount of serum available warrants it.

4.5.1.1 Insert the sharp end into one of the outlet ports in top of the bag.

4.5.1.2 Close tubing with thumb roller on tubing.

4.5.1.3 Press bag with plasma extractor.

4.5.1.4 Hold open end of tubing over prelabeled Wheaton bottles.

4.5.1.5 Open tubing and put 5 ml serum in "S3" bottle, 10 ml in "S4" and completely fill "S1" 4 oz bottle. Do not use "S2" bottle unless you have left over serum.

4.5.1.6 Extract only the serum being careful that cells do not enter the bottle. Recap and tighten. Crimp on aluminum caps to S3 and S4.

4.5.1.7 Log in the serum samples and store at -70° C until shipment.

5.0 SHORT DRAWS

5.1 In the event of a short draw, the participant involved maybe drawn again thus having 2 smaller units. The units from these should be treated as all the others with regard
to processing. Also, when aliquotting serum into the Wheaton bottles they may be pooled from both units.

6.0 MAILING OF SAMPLES

6.1 Frozen samples are mailed weekly to Brooks AFB,TX via Airborne overnight mail. See Mailouts Policy and Procedure.

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POLICIES AND PROCEDURES

Scripps Clinic
Department of Pathology
10666 N. Torrey Pines Road
La Jolla CA 92037

LABORATORY SECTION: **SPECIMEN CONTROL**
TITLE: **AFHS - DIOXIN MAILOUTS TO BROOK AFB**
P.P. NUMBER: ISSUE DATE: 4/20/92 REVISION DATE: 3/97

1.0 PURPOSE:

1.1 Procedure for mailing out Wheaton bottles with serum for dioxin testing to Brooks AFB.

2.0 SCOPE:

2.1 Applies to all medical technicians and technologists involved in the mailing of AFHS serum samples.

3.0 PROCEDURE

3.1 Serum drawn for dioxin testing will be mailed out once a week on each of the designated dioxin participant from the previous week.

3.2 Specimens will be packaged and mailed each Tuesday and will include all specimens drawn on the participants of the previous two groups.

3.3 Each participant will have three Wheaton bottles sent. (In some instances, there may be four Wheaton bottles on a participant.)

3.4 Shipment

3.4.1 The set of 3 aliquots will be removed from the -70°C freezer.

3.4.2 The aliquots will be placed in a 4" x 71/2" bubble pack bag. Each participant will have 2 bags. The 5 ml and 10 ml Wheaton bottles will be placed in one bubble pack per participant. The one 120 ml Wheaton bottle will be placed in a separate bubble pack bag. These aliquots will be placed in a bubble pack lined styrofoam shipping container. A third bag will be used if there are 4 Wheaton bottles on a participant.

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Sharon Boelmer 3/6/97 MT(ASCP)		
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3.4.3 As each of the participants are packed for shipping, they will be logged on the shipping list. This list will include the participant's name, age, ID# and accession number. The shipping list will have a comment section for any unusual occurrences, i.e., short draw, etc. Make a copy of shipping list and give to Sharon Bodmer.

3.4.4 Once all specimens are packed, add a sufficient amount of dry ice (approximately 15 lbs) above the specimens to keep them frozen for overnite shipment. Buffer package with additional bubble pack as needed.

3.4.5 Place the shipping list in a zip lock baggy and place inside the shipping box. Close the box and seal it with strapping tape.

3.4.4.1 Aside from sending the shipping list with the specimens, Fax a copy to Brooks AFB, attention Vince Elequin at (210) 536-3567.

3.4.6 Specimens will be mailed via FED EX overnight mail.

3.4.5.1 Fill out the overnite mail slip as follows:

AL/AOEP
2606 Doolittle Road
Building 808
Brooks AFB, TX 78235-5250
ATTN: Vince Elequin

This will be billed to acct. #20-227-7530

In comment section of the mailing slip, write in "Diagnostic Specimens" and indicate on "Dry Ice".

3.4.7 Once the shipping box is securely taped and mailing slip filled out, transport to shipping department before 1430 for shipping.

3.5 Procedural note

3.5.1 Specimen processing will be given a list of participants that require dioxin draws. If these participants are not drawn for any reason, i.e. Hemoglobin <12.5 mg/dl, they should be placed on the shipping list with their appropriate group and the reason for a non-draw placed in the comment section. The reason for a non-draw will be communicated from the AFHS nurse coordinator to the Laboratory Services Coordinator to the laboratory staff.

CONTACT PERSON: Sharon Bodmer
PHONE NUMBER: (619) 554-9552

GROUP # ______________________
PREPARED BY: ______________________
DATE SHIPPED: ______________________
TOTAL: ______________________

AFHS DIOXIN SHIPPING LIST
BOTTLES

PARTICIPANT'S NAME	CASE ID NUMBER	ACCESSION NUMBER	AGE	S1	S2	S3	S4	COMMENTS

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APPENDIX B

APPENDIX B. PHYSICAL EXAMINATION METHODOLOGY

This appendix contains the following items:

1. The Examiners' Handbook

2. The data collection forms.

ADDENDUM A

STATEMENT OF WORK

FOR THE

AIR FORCE HEALTH STUDY

1997 FOLLOW-UP EXAMINATION

AIR FORCE HEALTH STUDY
EXAMINERS HANDBOOK

3 July 1996
(Statement of Work Updates through 30 April 1999 included)

A. GENERAL INSTRUCTIONS

The Air Force Health Study is a multiyear prospective study to determine whether Air Force personnel who were engaged with spraying herbicides in Vietnam have developed adverse health effects from exposure to herbicides and their contaminant, 2,3,7,8-tetrachlorodibenzo-p-dioxin (dioxin). Detailed surveys of the scientific literature have been used to design the questionnaires, the physical examination protocol, and select laboratory tests.

This phase of the study involves a follow-up cross-sectional assessment of each subject's health at the time of the examination. It is important that examiners remain unaware of the subject's exposure status (Ranch Hand, Comparison). The physician examiner is tasked to examine each subject and objectively record findings. The examining physician is not, and cannot be expected, to arrive at any definitive diagnoses, since the full history and physical examination findings and laboratory results will not be available. Medical history, laboratory results, and physical examination findings will be evaluated by an independent diagnostician employed by the contractor. The diagnostician will formulate diagnoses and differential diagnoses, if appropriate. Additional procedures to treat or evaluate emergency or urgent medical conditions will be directed only by the diagnostician. In addition, the diagnostician will present a detailed analysis and debriefing to each study subject and provide a copy of the analysis to the subject's personal physician, if authorized by the subject.

The physicians performing examinations for the study should be aware that the report of the examination will become a permanent record. The report will be referenced not only in the near future as the cross-sectional data is analyzed, but also during future follow-up phases of the study. These examinations will define the health status of the subjects at a point in time and will establish the presence or absence of abnormal physical findings. After statistical review of the study groups, these findings may permit definition of chronic or latent effects due to exposure. An inaccurate examination may lead to fallacious results in two ways: a presumed syndrome may be defined which does not in fact exist, or a syndrome which in fact exists may not be defined with enough validity to warrant further action.

The examining physician is responsible for recording a complete and detailed report of the physical examination. In this role, the examining physician is tasked with collecting evidence of the presence or absence of physical signs of abnormality only. All items on the physical examination report form must be completed. It is imperative that physicians make such additional remarks as may be required to adequately describe existing physical abnormalities. Since clinical endpoints have not been well defined following exposure to Agent Orange, the examining physician and the diagnostician must not definitively ascribe abnormalities to herbicide exposure during the course of the examination or during the debriefings. If, during the examination, the physician discovers evidence of acute serious illness requiring immediate treatment, the normal emergency or urgent care procedure of the medical facility would apply. The Air Force is not responsible for the cost of such emergency or urgent care.

The debriefing physician shall ask each participant if he received additional testing or additional medical treatment during the physical examination time period and shall annotate any such circumstances or results on the debriefing form. The ultimate value of the study will lie in the collection of complete, accurate and, whenever possible, quantitative data permitting the most stringent and powerful statistical

analysis. For this reason, the physical examination protocol requires, whenever possible, exact measurements and well defined semi-quantitative indicators of abnormalities.

B. CONDUCT OF THE EXAMINATION

1. Overview

Upon arrival at the examining facility, the subject should be briefed by a representative of the contractor on the appointments that have been arranged, their times, and locations. Consent forms covering all examination procedures will be provided to each subject. The subject may decline to participate in any individual portion of the examination, even if he previously signed a consent form.

The examination will be conducted in a manner identical to that used in prior phases of the study and in accord with detail in subsequent sections of this handbook and the Statement of Work.

2. General Physical Examination

The general physical examination shall include an assessment of

1. Appearance (well nourished, obese, under nourished)
2. Appearance relative to stated age (same as, older than, younger than)
3. Appearance of illness or distress (no, yes)
4. Hair distribution (normal, abnormal)
5. Vital signs (height in centimeters, weight undressed in kilograms, oral temperature)
6. Systolic and diastolic blood pressure
7. Pulse rate
8. Premature beats per minute
9. Pulse diagnosis (regular, irregular, irregularly irregular)
10. An eye examination (funduscopic and external observation)
11. An ENT/neck examination
12. A thorax and lung examination
13. Waist, chest and neck measurements in centimeters
14. A heart examination including an overall diagnosis (normal, abnormal, refused)
15. An examination of the abdomen, extremities and peripheral pulses, musculature and spine
16. An examination of extremities
17. An examination of peripheral pulses
18. An examination of musculature
19. An examination of the spine
20. An examination of the genitourinary system
21. A rectal examination
22. An assessment of the lymph nodes (normal, enlarged, tender, hard, fixed, confluent, other)
23. A summary of follow-up indicated or recommended.

3. Dermatologic Examination And Biopsy

The examination shall include

1. An examination of the skin
2. Skin biopsy, if indicated
3. Physical features
4 Mapping of lesions on an anatomical chart.

4. Neurological Examination

The examination shall include

1. An examination of the head and neck
2. An examination of motor systems
3. An examination of muscle status
4. An assessment of abnormal movements
5. An assessment of tremors
6. An assessment of coordination
7. An assessment of deep tendon reflexes
8. An assessment of cranial nerves and mental status
9. An assessment of meningeal irritation and sensory system
10. An examination of cranial nerves (I, VII)
11. An examination of cranial nerves (II)
12. An examination of cranial nerves (III, IV, VI)
13. An examination of cranial nerves (V, IX, XI, XII)
14. An impression of the entire neurological examination.

5. Psychological Testing

The Symptom Check List-90-Revised (SCL-90-R) will be given to all study subjects. This self-administered test was chosen to ensure adequate analysis of alleged psychological manifestations of herbicide toxicity. The psychologist in charge will interpret the results of the test, record those interpretations on a form, and provide them to the debriefing physician. The contractor shall forward all test materials as scored with annotations, interpretations, and impressions to the diagnostician for inclusion in the subject's file.

6. Electrocardiogram

A standard 12-lead scalar electrocardiogram is required. If an arrhythmia is observed, a 1-minute rhythm strip is additionally requested. This electrocardiogram will be accomplished after a minimum 4-hour abstinence from smoking, food, and liquid intake. The tracing should be mounted in the usual manner of the laboratory for the recorder used. The electrocardiograms will be interpreted by cardiologists at the examination facility. Forward the mounted tracing and rhythm strip, if obtained, to the diagnostician.

7. Pulmonary Function Testing

Standard evaluation of pulmonary function will be conducted on each subject following at least 4 hours abstention from the use of tobacco products and will include, as minimum, forced expiratory volume at 1 second, total vital capacity, and the ratio of the two measurements.

8. Automated Blood Pressure Determination

An electronic device will be used to measure blood pressure. The device to be used will be selected by the contractor, subject to approval by the Air Force.

9. Stool Examination For Occult Blood

Three stool smears from each subject will be tested for the presence of occult blood. Subjects with positive tests will be advised and appropriate follow-up will be arranged.

10. Radiographic Examination

A standard 14×17 inch, standing, roentgenogram in the posterior-anterior (PA) position will be administered to all subjects. A board-certified radiologist at the examining facility will interpret the roentgenogram, record the results, and forward them to the diagnostician.

11. Doppler Testing Of Peripheral Pulses

A Doppler device shall be used to quantitatively measure peripheral pulses. This procedure shall be conducted after a minimum of 4 hours abstinence from smoking.

12. Measurement Of Height And Weight

The contractor shall determine the height in meters and weight in kilograms following a standard protocol on each subject. The contractor also shall measure the circumference of the waist at the navel and the circumference of the neck in centimeters.

13. Adipose Tissue Samples

The contractor shall:

1. Collect 10–15 gm fat tissue by liposuction procedure or any other alternative method.
2. Rinse one time with ice-cold normal phosphate-buffered saline (PBS).
3. Remove any excess of PBS solution from the tissue using paper towel.
4. Either snap freeze immediately in liquid nitrogen or keep it on ice until snap freezing (no longer than 30 minutes).
5. Store at –80 °C until delivery to Brooks Air Force Base.

14. Laboratory Procedures – General Instructions

On the first day, the subject should report in the morning in a fasting state having had only water after midnight. Blood for the serum dioxin measurement will be drawn on 650 selected subjects who consent to this procedure. Sufficient blood for the dioxin measurement will be drawn to bring the total volume collected over the 2 days to not more than 450 cc from these volunteers.

All study subjects should be informed that they should abstain from alcohol for 24 hours prior to the start of the physical examination.

15. Laboratory Procedures - Specific Tests To Be Performed

1. Erythrocyte sedimentation rate (mm/hr)
2. Prostate specific antigen (ng/ml)
3. AST (U/L)
4. ALT (U/L)
5. GGT (U/L)
6. Alkaline phosphatase (U/L)
7. Total bilirubin (mg/dl)
8. Direct bilirubin (mg/dl)
9. Lactic dehydrogenase (U/L)
10. Cholesterol (mg/dl)
11. HDL cholesterol (mg/dl)
12. Triglycerides (mg/dl)
13. Creatine phosphokinase (U/L)
14. Serum amylase (U/L)
15. Antibodies for hepatitis A, B, C and D
16. Serological evidence of prior hepatitis B infection (positive anti-HB_s or anti-HB_c)
17. Protein profile: pre-albumin (mg/dl)
18. Protein profile: albumin (mg/dl)
19. Protein profile: α-1-glycoprotein (mg/dl)
20. Protein profile: α-1-antitrypsin (mg/dl)
21. Protein profile: α-2-macroglobulin (mg/dl)
22. Protein profile: apolipoprotein (mg/dl)
23. Protein profile: C3 complement (mg/dl)
24. Protein profile: C4 compliment (mg/dl)
25. Protein profile: haptoglobin (mg/dl)
26. Protein profile: transferrin (mg/dl)
27. Red blood cell count (million/cu mm)
28. White blood cell count (thousand/cu mm)
29. Hemoglobin (gm/dl)
30. Hematocrit (percent)
31. Platelet count (thousand/cu mm)
32. Prothrombin time (seconds)
33. RBC morphology (abnormal, normal)
34. Absolute neutrophils (segs) (million/cu mm)
35. Absolute neutrophils (bands) (million/cu mm)
36. Absolute lymphocytes (million/cu mm)
37. Absolute monocytes (million/cu mm)
38. Absolute eosinophils (million/cu mm)
39. Absolute basophils (million/cu mm)
40. Urinary occult blood (RBC/HPF)
41. Urinary protein (present, absent)
42. Urine white blood cell count (WBC/HPF)
43. Serum creatinine (mg/dl)
44. Urine specific gravity
45. Anti-thyroid antibodies (present, absent)
46. Thyroid stimulating hormone (μIU/ml)
47. T_4 (μg/dl)

48. Fasting glucose (mg/dl)
49. Fasting urinary glucose (present, absent)
50. Serum insulin (μIU/ml)
51. α-1-C hemoglobin (percent)
52. Luteinizing hormone (mIU/ml)
53. Follicle stimulating hormone (mIU/ml)
54. Total testosterone (ng/dl)
55. Free testosterone (pg/ml)
56. Estradiol (pg/ml)
57. Two-hour postprandial glucose (mg/dl) (non-diabetics only)
58. Two-hour postprandial urinary glucose (present, absent) (non-diabetics only)
59. CD3+ (T Cells) (cells/cu mm and percent)
60. CD4+ (Helper T Cells) (cells/cu mm and percent)
61. CD8+ (Suppressor T Cells) (cells/cu mm and percent)
62. CD3+CD8+ (Suppressor T Cells) (cells/cu mm and percent)
63. CD16+56+(CD3–) (Natural Killer Cells) (cells/cu mm and percent)
64. CD20+ (B Cells) (cells/cu mm and percent)
65. CD3+CD4+ (Helper T Cells) (cells/cu mm and percent)
66. CD45+(CD14–) (used as quality control marker)
67. Absolute lymphocytes (cells/cu mm)
68. IgG (mg/dl)
69. IgM (mg/dl)
70. IgA (mg/dl)
71. Lupus panel: ANA test (present, absent)
72. Lupus panel: ANA thyroid microsomal antibody (present, absent)
73. Lupus panel: MSK smooth muscle antibody (present, absent)
74. Lupus panel: MSK mitrochondrial antibody (present, absent)
75. Lupus panel: MSK parietal antibody (present, absent)
76. Lupus panel: Rheumatoid factor (present, absent)

PARTICIPANT LABEL	CASE NUMBER	GROUP NUMBER
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	EXAMINER I.D.
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨

UNITED STATES AIR FORCE HEALTH STUDY

YEAR 15 FOLLOW UP

FORM AFHS-3A PHYSICAL EXAMINATION (PART 1) (SHEET 1 OF 2)

GENERAL PHYSICAL APPEARANCE

APPEARANCE	APPEARANCE VS STATED AGE	APPEARANCE OF ILLNESS OR DISTRESS	HAIR DISTRIBUTION
◯ WELL NOURISHED	◯ SAME AS	◯ NO	◯ NORMAL
◯ OBESE	◯ OLDER THAN		
◯ UNDER NOURISHED	◯ YOUNGER THAN	◯ YES	◯ ABNORMAL

Ⓨ Ⓝ COMMENTS?

NOTE: FILL IN VITAL SIGNS WITH MAXIMUM VALUES IF REFUSED.

VITAL SIGNS

HEIGHT CM	WEIGHT (UNDRESSED) KG	TEMPERATURE ORAL °F	SITTING BLOOD PRESSURE NONDOMINANT ARM, HEART LEVEL SYSTOLIC	DIASTOLIC	PULSE RATE
⓪⓪	⓪⓪⓪⓪	⑨⓪⓪	⓪⓪⓪	⓪⓪⓪	⓪⓪⓪
①①①	①①①①	⑩①①	①①①	①①①	①①①
②②②	②②②②	②②	②②②	②②	②②②
③③③	③③③③	③③	③③	③③	③③③
④④	④④④	④④	④④	④④	④④
⑤⑤	⑤⑤⑤	⑤⑤	⑤⑤	⑤⑤	⑤⑤
⑥⑥	⑥⑥⑥	⑥⑥	⑥⑥	⑥⑥	⑥⑥
⑦⑦	⑦⑦⑦	⑦⑦	⑦⑦	⑦⑦	⑦⑦
⑧⑧	⑧⑧⑧	⑧⑧	⑧⑧	⑧⑧	⑧⑧
⑨⑨	⑨⑨⑨	⑨⑨	⑨⑨	⑨⑨	⑨⑨

Ⓨ Ⓝ COMMENTS?

Ⓨ Ⓝ IS PARTICIPANT TAKING SYSTEMIC CORTICOSTERIODS OR IMMUNOSUPPRESSANTS?
SPECIFY NON-COMPLIANCE AND / OR MEDICATION(S), DOSAGE(S) & FUNCTION(S) BELOW:

EYES

SUMMARY

◯ NORMAL

◯ ABNORMAL

◯ REFUSED

◯ LEFT EYE ABSENT

◯ RIGHT EYE ABSENT

FUNDOSCOPIC EXAM

YES	NO		YES	NO	
Ⓨ	Ⓝ	↑ LIGHT REFLEX	Ⓨ	Ⓝ	HEMORRHAGES
Ⓨ	Ⓝ	A-V NICKING	Ⓨ	Ⓝ	EXUDATES
Ⓨ	Ⓝ	ARTERIOLAR SPASM	Ⓨ	Ⓝ	DISK PALLOR
Ⓨ	Ⓝ	PAPILLEDEMA	Ⓨ	Ⓝ	↑ CUPPING
		Ⓑ Ⓛ Ⓡ FUNDI WERE VISUALIZED	Ⓨ	Ⓝ	DIABETIC RETINOPATHY

(B = BOTH, L = LEFT ONLY, R = RIGHT ONLY)

EXTERNAL OBSERVATION

YES	NO	
Ⓨ	Ⓝ	ARCUS SENILIS PRESENT
Ⓨ	Ⓝ	ABNORMAL OCULAR PIGMENTATION

PHYSICIAN'S PRINTED NAME

DATE:

Ⓨ Ⓝ COMMENTS?

FORM QA AUDIT BY: ①②③④⑤⑥ INITIALS:

DATE:

PARTICIPANT LABEL	CASE NUMBER	GROUP NUMBER
	0 1 2 3 4 5 6 7 8 9	0 1 2 3 4 5 6 7 8 9
	0 1 2 3 4 5 6 7 8 9	0 1 2 3 4 5 6 7 8 9
	0 1 2 3 4 5 6 7 8 9	EXAMINER I.D.
	0 1 2 3 4 5 6 7 8 9	0 1 2 3 4 5 6 7 8 9
	0 1 2 3 4 5 6 7 8 9	0 1 2 3 4 5 6 7 8 9
	0 1 2 3 4 5 6 7 8 9	0 1 2 3 4 5 6 7 8 9

FORM AFHS-3A PHYSICAL EXAMINATION (PART 1) (SHEET 2 OF 2)

YEAR 15 FOLLOW UP

CODES Ⓝ = NO OR NONE Ⓨ = YES Ⓡ = REFUSED Ⓧ = COULD NOT EXAMINE Ⓛ = LEFT Ⓡ = RIGHT

ENT/NECK

ENT ARE
- ◯ NORMAL
- ◯ ABNORMAL
- ◯ REFUSED

	LEFT	RIGHT
TYMPANIC MEMBRANE INTACT?	N Y X	N Y X
EAR IRRIGATED TO REMOVE WAX?	N Y	N Y
NASAL MUCOSA ULCERATED?	N Y X	N Y X

Y N COMMENTS?

NECK AREA IS
- ◯ NORMAL
- ◯ ABNORMAL
- ◯ REFUSED

PAROTID GLAND RELATED?	N Y	N Y
CAROTID BRUIT PRESENT?	N Y	N Y
CAROTID PULSE IS:	N D A	N D A

(N = NORMAL D = DIMINISHED A = ABSENT)

THYROID GLAND	PALPABLE	ENLARGED	NODULES	TENDER	OTHER
	N Y	N Y	N Y	N Y	N Y

Y N COMMENTS?

THORAX AND LUNGS

- ◯ NORMAL
- ◯ ABNORMAL
- ◯ REFUSED

Y N COMMENTS?

- Y N ASYMMETRICAL EXPANSION
- Y N HYPERRESONANCE
- Y N DULLNESS
- Y N WHEEZES
- Y N RALES
- ← (NOTE LOCATION)
- Y N SUSPECTED COPD
- ← (DESCRIBE)

CIRCUMFERENCE (CM)

WAIST	CHEST AT NIPPLE LEVEL: EXPIRATION	CHEST AT NIPPLE LEVEL: INSPIRATION	NECK
0 0 0	0 0 0	0 0 0	0 0 0
1 1 1	1 1 1	1 1 1	1 1 1
2 2 2	2 2	2 2	2 2 2
3 3 3	3 3	3 3	3 3 3
4 4	4 4	4 4	4 4
5 5	5 5	5 5	5 5
6 6	6 6	6 6	6 6
7 7	7 7	7 7	7 7
8 8	8 8	8 8	8 8
9 9	9 9	9 9	9 9

HEART

HEART EXAM IS:
- ◯ NORMAL
- ◯ ABNORMAL
- ◯ REFUSED

MURMUR?
- ◯ NO
- ◯ YES, PROBABLY FUNCTIONAL
- ◯ YES, SUSPECT ORGANIC
- ◯ YES, ORGANIC

INDICATE CHEST AREA(S) TO WHICH MURMUR WAS PROJECTED MOST INTENSELY.

(MARK Ns IF NO MURMUR)

	SYSTOLIC	DIASTOLIC
AORTIC	N Y	N Y
PULMONIC	N Y	N Y
APEX	N Y	N Y
LLSB	N Y	N Y

	S1	S2	S3	S4
ABNORMAL HEART SOUNDS?	N Y	N Y	N Y	N Y

- Y N DISPLACED APICAL IMPULSE?
- Y N PRECORDIAL THRUST?

Y N HEART COMMENTS?

FORM QA AUDIT BY: 1 2 3 4 5 6 INITIALS:

DATE:

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PARTICIPANT LABEL	CASE NUMBER	GROUP NUMBER
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	EXAMINER I.D.
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨

UNITED STATES AIR FORCE HEALTH STUDY

FORM AFHS-3B PHYSICAL EXAMINATION (PART 2) (SHEET 1 OF 2)

YEAR 15 FOLLOW UP

ABDOMEN

Ⓨ Ⓝ ABDOMEN ABNORMALITY COMMENTS?

○ NORMAL
○ ABNORMAL
○ REFUSED

YES	NO	
○	○	HEPATOMEGALY
○	○	LIVER TENDERNESS
○	○	SPLENOMEGALY
○	○	SPLEEN TENDERNESS
○	○	OTHER MASS? →

TOTAL LIVER SPAN ⓪①②③④ CM ⓪①②③④⑤⑥⑦⑧⑨

Ⓨ Ⓝ MASS SIZE, UNITS, LOCATION, TYPE, COMMENT?

EXTREMITIES

	AMPUTATION(S)	PITTING EDEMA	NON-PITTING EDEMA	CLUBBED NAILS	VARICOSITIES	TOE HAIR LOSS
UPPER LIMBS	ⓃⓁⓇ	ⓃⓁⓇ	ⓃⓁⓇ	ⓃⓁⓇ	ⓃⓁⓇ	
LOWER LIMBS	ⓃⓁⓇ	ⓃⓁⓇ	ⓃⓁⓇ	ⓃⓁⓇ	ⓃⓁⓇ	ⓃⓁⓇ

(N = NONE OR NORMAL FOR BOTH LIMBS, L = LEFT LIMB ONLY, R = RIGHT LIMB ONLY)

EXTREMITY EXAM WAS: ○ NORMAL ○ ABNORMAL ○ REFUSED

Ⓨ Ⓝ DESCRIBE ABSENCES & / OR ABNORMALITIES

PERIPHERAL PULSES

ⓃⓁⓇ FEMORAL BRUIT(S) PRESENT?
(N = NONE, L = LEFT, R = RIGHT)

	RADIAL LEFT	RADIAL RIGHT	FEMORAL LEFT	FEMORAL RIGHT	POPLITEAL LEFT	POPLITEAL RIGHT	DORSALIS PEDIS LEFT	DORSALIS PEDIS RIGHT	POSTERIOR TIBIAL LEFT	POSTERIOR TIBIAL RIGHT
NORMAL	○	○	○	○	○	○	○	○	○	○
DIMINISHED	○	○	○	○	○	○	○	○	○	○
ABSENT	○	○	○	○	○	○	○	○	○	○
COULD NOT EXAMINE	ⓧ	ⓧ	ⓧ	ⓧ	ⓧ	ⓧ	ⓧ	ⓧ	ⓧ	ⓧ

Ⓨ Ⓝ PULSE COMMENTS

MUSCULATURE

○ NORMAL
○ ABNORMAL
○ REFUSED

	NO	YES	CNE
STRAIGHT LEG RAISE ABNORMAL?	○	○	ⓧ
ANY WEAKNESS NOTED?	○	○	ⓧ
ANY TENDERNESS NOTED?	○	○	ⓧ
ANY ATROPHY NOTED?	○	○	ⓧ
ABNORMAL CONSISTENCY?	○	○	ⓧ
OTHER ABNORMALITY?	○	○	ⓧ

Ⓨ Ⓝ COMMENTS?

SPINE

○ NORMAL
○ ABNORMAL
○ REFUSED

	NO	YES	CNE
ANY SCOLIOSIS NOTED?	○	○	ⓧ
ANY KYPHOSIS NOTED?	○	○	ⓧ
PELVIC TILT NOTED?	○	○	ⓧ
↓ RANGE OF MOTION?	○	○	ⓧ

SPINAL TENDERNESS
○ NONE NOTED
○ CERVICAL AREA
○ THORACIC AREA
○ LUMBAR AREA
○ SACRAL AREA

Ⓨ Ⓝ COMMENTS?

FORM QA AUDIT BY: ①②③④⑤⑥ INITIALS:

DATE:

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PARTICIPANT LABEL	CASE NUMBER	GROUP NUMBER
	0 1 2 3 4 5 6 7 8 9 (×6)	0 1 2 3 4 5 6 7 8 9 (×2)
		EXAMINER I.D. 0 1 2 3 4 5 6 7 8 9 (×3)

FORM AFHS-3B PHYSICAL EXAMINATION (PART 2) (SHEET 2 OF 2)

YEAR 15 FOLLOW UP

GENITOURINARY EXAM

(PE PART 2 CONTINUED)

GENITOURINARY EXAM

- ○ NORMAL
- ○ ABNORMAL
- ○ REFUSED

TESTES

	NORMAL	ENLARGED	NODULE	ATROPHIC	ABSENT	OTHER
LEFT	○	○	○	○	○	○
RIGHT	○	○	○	○	○	○

YES	NO	REFUSED	
Y	N	R	RIGHT INGUINAL HERNIA?
Y	N	R	LEFT INGUINAL HERNIA?
Y	N	R	SCROTAL MASS PRESENT?

YES	NO	REFUSED	
Y	N	R	VARICOCELE
Y	N	R	EPIDIDYMAL ABNORMALITY

0 1 2 3 4 5 6 7 8 + SCROTAL MASS SIZE (DIAMETER IN CM)

Y N COMMENTS:

RECTAL EXAM

RECTAL EXAM

- ○ NORMAL
- ○ ABNORMAL
- ○ REFUSED

HEMORRHOIDS	NONE APPARENT	REFUSED	BLEEDING	THROMBOSED	OTHER
EXTERNAL	○	○	○	○	○
INTERNAL	○	○	○	○	○

YES	NO	REFUSED	
○	○	○	PROSTATIC ENLARGEMENT?
○	○	○	RECTAL MASS(ES)?

Y N COMMENTS?

LYMPH NODES

- ○ NORMAL
- ○ ABNORMAL
- ○ REFUSED

	NORMAL	ENLARGED	TENDER	HARD	FIXED	CONFLUENT	OTHER
CERVICAL	○	○	○	○	○	○	○
OCCIPITAL	○	○	○	○	○	○	○
SUPRACLAVICULAR	○	○	○	○	○	○	○
AXILLARY	○	○	○	○	○	○	○
EPITROCHLEAR	○	○	○	○	○	○	○
INGUINAL	○	○	○	○	○	○	○
FEMORAL	○	○	○	○	○	○	○

Y N COMMENTS:

SUMMARY OF FOLLOW-UP INDICATED OR RECOMMENDED

SUMMARY OF FINDINGS ENTIRE EXAM WAS:

- ○ ALL NORMAL
- ○ NORMAL WITH NOTED VARIATIONS
- ○ ABNORMAL AS SUMMARIZED
- ○ REFUSED ENTIRE EXAM

Y N ANY OTHER TESTS INDICATED?
Y N ANY OTHER TESTS ORDERED?
Y N OTHER TESTS DESCRIBED?

Y N COMMENTS:

PRINTED NAME OF EXAMINING PHYSICIAN	INITIALS / DATE	FORM QA AUDIT BY: 1 2 3 4 5 6	INITIALS:
		DATE:	

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PARTICIPANT LABEL	CASE NUMBER	GROUP NUMBER
	⓪①②③④⑤⑥⑦⑧⑨ (×6 rows)	⓪①②③④⑤⑥⑦⑧⑨ (×2 rows)
		EXAMINER I.D.
		⓪①②③④⑤⑥⑦⑧⑨ (×3 rows)

FORM AFHS-4A DERMATOLOGIC EXAMINATION AND BIOPSY

YEAR 15 FOLLOW UP

FOR POSITIVE FINDINGS NOTE TYPE AND LOCATION ON ANATOMIC CHART AND DARKEN THE APPROPRIATE CIRCLE BELOW

SKIN

EXAM WAS: ○ NORMAL ○ NORMAL WITH RESULTS ○ ABNORMAL ○ REFUSED | ANATOMICAL CHART USED? Ⓨ Ⓝ

YES	NO	TYPE		YES	NO	TYPE	
○	○	1	COMEDONES	○	○	17	ORAL MUCOSAL ABNORMALITY
○	○	2	ACNEIFORM LESIONS	○	○	18	FINGER NAIL ABNORMALITY
○	○	3	ACNEIFORM SCARS	○	○	19	TOE NAIL ABNORMALITY
○	○	4	DEPIGMENTATION	○	○	20	DERMATOGRAPHIA
○	○	5	INCLUSION CYSTS	○	○	21	SUSPECTED BASAL CELL CARCINOMA
○	○	6	CUTIS RHOMBOIDALIS	○	○	22	SUSPECTED SQUAMOUS CELL CARCINOMA
○	○	7	HYPERPIGMENTATION	○	○	23	ATYPICAL/UNUSUAL NEVUS
○	○	8	JAUNDICE	○	○	24	VITILIGO
○	○	9	SPIDER ANGIOMATA	○	○	25	TINEA PEDIS
○	○	10	PALMAR ERYTHEMA	○	○	26	INTERTRIGO
○	○	11	SUSPECTED MELANOMA	○	○	27	LIPOMA
○	○	12	PALMAR KERATOSES	○	○	28	ECZEMA
○	○	13	ACTINIC KERATOSES	○	○	29	PSORIASIS
○	○	14	PETECHIAE	○	○	30	SEBORRHEIC DERMATITIS
○	○	15	ECCHYMOSES	○	○	31	OTHER ABNORMALITY(IES)
○	○	16	CONJUNCTIVAL ABNORMALITY				

SKIN BIOPSY

○ BIOPSY NOT INDICATED
○ BIOPSY INDICATED, IF SO → ○ BIOPSY REFUSED
→ ○ BIOPSY PERFORMED, IF SO → # SAMPLES ⓪①②③④⑤⑥⑦⑧⑨
→ YES ○ CONSENT FORM OBTAINED
→ ○ REFERRED

Ⓨ Ⓝ SAMPLE # TYPE AND LOCATION CODE(S)	Ⓨ Ⓝ COMMENT(S)/SUSPECTED DIAGNOSIS

PRINTED NAME OF EXAMINING PHYSICIAN	INITIALS / DATE	FORM QA AUDIT BY: ①②③④⑤⑥ INITIALS: DATE:

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PARTICIPANT LABEL	CASE NUMBER	GROUP NUMBER
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	EXAMINER I.D.
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨

UNITED STATES AIR FORCE HEALTH STUDY

FORM AFHS-4B PHYSICAL FEATURES

YEAR 15 FOLLOW UP

Ⓨ Ⓝ Ⓧ WEARING COLORED OR TINTED CONTACTS?

EYE COLOR

	LEFT	RIGHT
BROWN	◯	◯
HAZEL	◯	◯
GREEN	◯	◯
GREY	◯	◯
BLUE	◯	◯
ABSENT	◯	◯

HAIR COLOR

SOLID COLOR ⟶ GREYS

BLACKS	① ㉞ ㊹ ㊿51 151
BROWNS	⑤ ⑪ ㊱ ㊳ ㊴ ㊽ 54
BLONDS	⑭ 103 101
REDS	㉝ ㉙
BALD	⓪ Ⓧ NOT NEEDED

(NOTE: 151 - BLACK AND GREY)

Ⓨ Ⓝ IS HAIR DYED OR ALTERED?

SKIN COLOR

NN

Ⓧ ① ② ③ ④ ⑤ ⑥ ⑦ ⑧ ⑨ ⑩ ⑪ ⑫

Ⓨ Ⓝ COMMENTS?

PRINTED NAME OF EXAMINING PHYSICIAN	INITIALS / DATE	FORM QA AUDIT BY: ① ② ③ ④ ⑤ ⑥ INITIALS: DATE:

Mark Reflex® by NCS MM212098-1 654321 GS99 Printed in U.S.A.

PARTICIPANT LABEL	CASE NUMBER	GROUP NUMBER
	⓪①②③④⑤⑥⑦⑧⑨ (×6)	⓪①②③④⑤⑥⑦⑧⑨ (×2)
		EXAMINER I.D. ⓪①②③④⑤⑥⑦⑧⑨ (×3)

YEAR 15 FOLLOW UP

FORM AFHS - 5 NEUROLOGIC EXAMINATION (SHEET 1 OF 2)

HEAD AND NECK

INSPECTION AND PALPATION

○ NORMAL
○ ABNORMAL

CNE	YES	NO	
Ⓧ	Ⓨ	Ⓝ	ASYMMETRY
Ⓧ	Ⓨ	Ⓝ	DEPRESSION
Ⓧ	Ⓨ	Ⓝ	SCAR
Ⓧ	Ⓨ	Ⓝ	OTHER

NECK RANGE OF MOTION

	NORMAL	DECEASED	CNE
LEFT	○	○	Ⓧ
RIGHT	○	○	Ⓧ
FORWARD	○	○	Ⓧ
BACKWARD	○	○	Ⓧ

Ⓨ Ⓝ COMMENTS

MOTOR SYSTEMS

GAIT

○ NORMAL
○ ABNORMAL
○ COULD NOT EXAMINE

Ⓨ Ⓝ BROAD BASED
Ⓨ Ⓝ SMALL STEPPED
Ⓨ Ⓝ ATAXIC
Ⓨ Ⓝ OTHER →

Ⓨ Ⓝ COMMENTS

ARM SWING MOVEMENT

	NORMAL	ABNORMAL	CNE
LEFT	○	○	Ⓧ
RIGHT	○	○	Ⓧ

HANDEDNESS

○ LEFT
○ RIGHT
○ BOTH

MUSCLE STATUS

BULK: ○ NORMAL ○ ABNORMAL

	NORMAL	CNE	DECREASED LEFT	DECREASED RIGHT	DECREASED BOTH	INCREASED LEFT	INCREASED RIGHT	INCREASED BOTH
TONE								
UPPER EXTREMITIES	○	Ⓧ	○	○	○	○	○	○
LOWER EXTREMITIES	○	Ⓧ	○	○	○	○	○	○
STRENGTH								
DISTAL WRIST EXTENSORS	○	Ⓧ	○	○	○			
ANKLE/TOE FLEXORS	○	Ⓧ	○	○	○			
PROXIMAL DELTOIDS	○	Ⓧ	○	○	○			
HIP FLEXORS	○	Ⓧ	○	○	○			

Ⓨ Ⓝ COMMENTS

ABNORMAL MOVEMENTS

Ⓨ Ⓝ TICS, CHOREAS FASICULATIONS ①②③④ Ⓨ Ⓝ TENDERNESS ①②③④ Ⓨ Ⓝ COMMENTS

TREMOR(S)

	UPPER LEFT	UPPER RIGHT	LOWER LEFT	LOWER RIGHT
NO TREMOR	○	○	○	○
RESTING	○	○	○	○
ESSENTIAL	○	○	○	○
INTENTION	○	○	○	○
OTHER	○	○	○	○

EXTREMITY

Ⓨ Ⓝ COMMENTS

SPEECH

○ NORMAL ○ DYSARTHRIA
○ APHASIA ○ AGNOSIA
○ OTHER ABNORMALITY

Ⓨ Ⓝ COMMENTS

COORDINATION

	NORMAL	ABNORMAL LEFT	ABNORMAL RIGHT	ABNORMAL BOTH	CNE
1 EQUILIBRATORY (ROMBERG)	○				Ⓧ
2 FINGER-NOSE-FINGER	○	○	○	○	Ⓧ
3 HEEL-KNEE-SHIN	○	○	○	○	Ⓧ
4 HAND PRONATION/SUPINATION	○	○	○	○	Ⓧ
5 RAPID PATTING	○	○	○	○	Ⓧ

Ⓨ Ⓝ COMMENTS

DEEP TENDON REFLEXES

(0 = ABSENT, 1 = SLUGGISH, 2 = ACTIVE, 3 = VERY ACTIVE, X = CNE)

	LEFT ACTIVITY	CNE	RIGHT ACTIVITY	CNE
BICEPS	⓪①②③	Ⓧ	⓪①②③	Ⓧ
TRICEPS	⓪①②③	Ⓧ	⓪①②③	Ⓧ
PATELLAR	⓪①②③	Ⓧ	⓪①②③	Ⓧ
ACHILLES	⓪①②③	Ⓧ	⓪①②③	Ⓧ
BABINSKI	PRESENT ○ ABSENT ○	Ⓧ	PRESENT ○ ABSENT ○	Ⓧ

Ⓨ Ⓝ COMMENTS

CLONUS

	LEFT NORMAL	LEFT TRANSIENT	LEFT SUSTAINED	CNE	RIGHT NORMAL	RIGHT TRANSIENT	RIGHT SUSTAINED	CNE
PATELLAR	○	○	○	Ⓧ	○	○	○	Ⓧ
ACHILLES	○	○	○	Ⓧ	○	○	○	Ⓧ

Ⓨ Ⓝ COMMENTS

FORM QA AUDIT BY: ①②③④⑤⑥ INITIALS:

DATE:

PARTICIPANT LABEL	CASE NUMBER	GROUP NUMBER
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	EXAMINER I.D.
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨

YEAR 15 FOLLOW UP

FORM AFHS - 5 NEUROLOGIC EXAMINATION (SHEET 2 0F 2)

CRANIAL NERVES AND MENTAL STATUS

CODES: Ⓧ = COULD NOT EXAMINE Ⓝ = NO; NOT NORMAL Ⓨ = YES, NORMAL
Ⓡ = DEVIATED TO RIGHT SIDE Ⓛ = DEVIATED TO LEFT SIDE

MENINGEAL IRRITATION AND SENSORY SYSTEM

	NORMAL	- ABNORMAL - LEFT	RIGHT	BOTH	CNE
STRAIGHT LEG RAISING	○	○	○	○	Ⓧ
LIGHT TOUCH	○	○	○	○	Ⓧ
PIN PRICK	○	○	○	○	Ⓧ
VIBRATION AT ANKLE (128 HZ)	○	○	○	○	Ⓧ
POSITION (GREAT TOE)	○	○	○	○	Ⓧ

Ⓨ Ⓝ COMMENTS

CRANIAL NERVES (I, VII)

LEFT	RIGHT	
Ⓧ Ⓝ Ⓨ	Ⓧ Ⓝ Ⓨ	SENSE OF SMELL PRESENT?
Ⓧ Ⓝ Ⓨ	Ⓧ Ⓝ Ⓨ	SMILE NORMAL?
Ⓧ Ⓝ Ⓨ	Ⓧ Ⓝ Ⓨ	PALPEBRAL FISSURE NORMAL?

Ⓨ Ⓝ COMMENTS (I, VII)

CRANIAL NERVES (II)

LEFT	RIGHT	
Ⓧ Ⓝ Ⓨ	Ⓧ Ⓝ Ⓨ	FUNDOSCOPIC EXAM NORMAL?
Ⓧ Ⓝ Ⓨ	Ⓧ Ⓝ Ⓨ	ABSENCE OF DISK PALLOR/ATROPHY?
Ⓧ Ⓝ Ⓨ	Ⓧ Ⓝ Ⓨ	ABSENCE OF EXUDATE?
Ⓧ Ⓝ Ⓨ	Ⓧ Ⓝ Ⓨ	ABSENCE OF PAPILLEDEMA?
Ⓧ Ⓝ Ⓨ	Ⓧ Ⓝ Ⓨ	ABSENCE OF HEMORRHAGE?

Ⓨ Ⓝ COMMENTS (II)

CRANIAL NERVES (III, IV, VI)

LEFT	RIGHT	
Ⓧ Ⓝ Ⓨ	Ⓧ Ⓝ Ⓨ	CONTACT LENS REMOVED?
Ⓧ Ⓝ Ⓨ	Ⓧ Ⓝ Ⓨ	VISUAL FIELDS NORMAL TO CONFRONTATION?
→	Ⓧ Ⓝ Ⓨ	→ PUPILS EQUAL SIZE? DIFFERENCE → ⓪①②③④ mm
Ⓧ Ⓝ Ⓨ	Ⓧ Ⓝ Ⓨ	PUPIL SHAPE/POSITION ROUND & NORMAL?
Ⓧ Ⓝ Ⓨ	Ⓧ Ⓝ Ⓨ	LIGHT REACTION NORMAL?
Ⓧ Ⓝ Ⓨ	Ⓧ Ⓝ Ⓨ	HORIZONTAL NYSTAGMUS
Ⓧ Ⓝ Ⓨ	Ⓧ Ⓝ Ⓨ	VERTICAL NYSTAGMUS
Ⓧ Ⓝ Ⓨ	Ⓧ Ⓝ Ⓨ	ROTARY NYSTAGMUS
Ⓧ Ⓝ Ⓨ	Ⓧ Ⓝ Ⓨ	EYEBALL POSITION NORMAL? →
Ⓧ Ⓝ Ⓨ	Ⓧ Ⓝ Ⓨ	PTOSIS ABSENT?
Ⓧ Ⓝ Ⓨ	Ⓧ Ⓝ Ⓨ	CORNEAL REFLEX NORMAL?

DRAW ABNORMAL POSITIONS

Ⓨ Ⓝ COMMENTS (III,IV, VI)

CRANIAL NERVES (V, IX, XI, XII)

LEFT	RIGHT	
Ⓧ Ⓝ Ⓨ	Ⓧ Ⓝ Ⓨ	TRIGEMINAL V1 SENSORY NORMAL?
Ⓧ Ⓝ Ⓨ	Ⓧ Ⓝ Ⓨ	TRIGEMINAL V2 SENSORY NORMAL?
Ⓧ Ⓝ Ⓨ	Ⓧ Ⓝ Ⓨ	TRIGEMINAL V3 SENSORY NORMAL?
Ⓧ Ⓝ Ⓨ	Ⓧ Ⓝ Ⓨ	PALATE REFLEX NORMAL?
Ⓨ Ⓝ	Ⓡ Ⓛ	TONGUE PROTRUDES TO MIDDLE, NOT DEVIATED?
Ⓨ Ⓝ	Ⓡ Ⓛ	TONGUE NORMAL, NOT ATROPHIED?
Ⓨ Ⓝ	Ⓡ Ⓛ	CLENCH JAW SYMMETRIC (NOT DEVIATED)?
Ⓨ Ⓝ	Ⓡ Ⓛ	PALATE & UVULA MOVEMENT (NOT DEVIATED)?

Ⓨ Ⓝ COMMENTS (V, IX, XI, XII)

Ⓨ Ⓝ MENTAL STATUS GROSSLY ORIENTED & NORMAL?

Ⓨ Ⓝ COMMENTS

IMPRESSION OF ENTIRE NEUROLOGIC EXAM

- ○ COMPLETELY NORMAL EXAM
- ○ NORMAL WITH MINOR VARIATIONS NOTED
- ○ ABNORMAL WITH NO FOLLOW-UP NEEDED
- ○ ABNORMAL WITH FOLLOW-UP RECOMMENDED

Ⓨ Ⓝ COMMENTS

PRINTED NAME OF EXAMINING PHYSICIAN/DATE

FORM QA AUDIT BY: ①②③④⑤⑥ INITIALS:

DATE:

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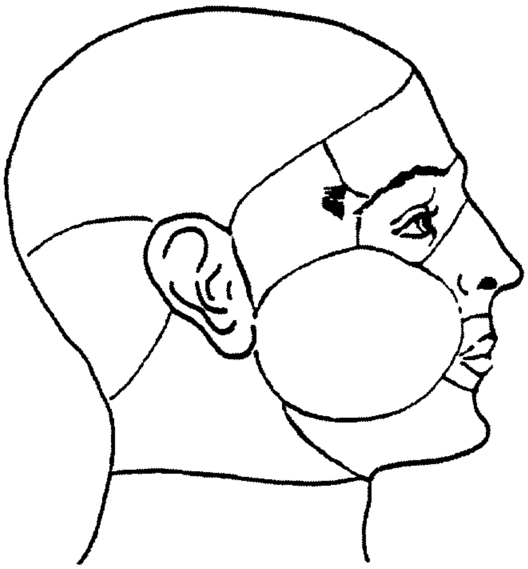
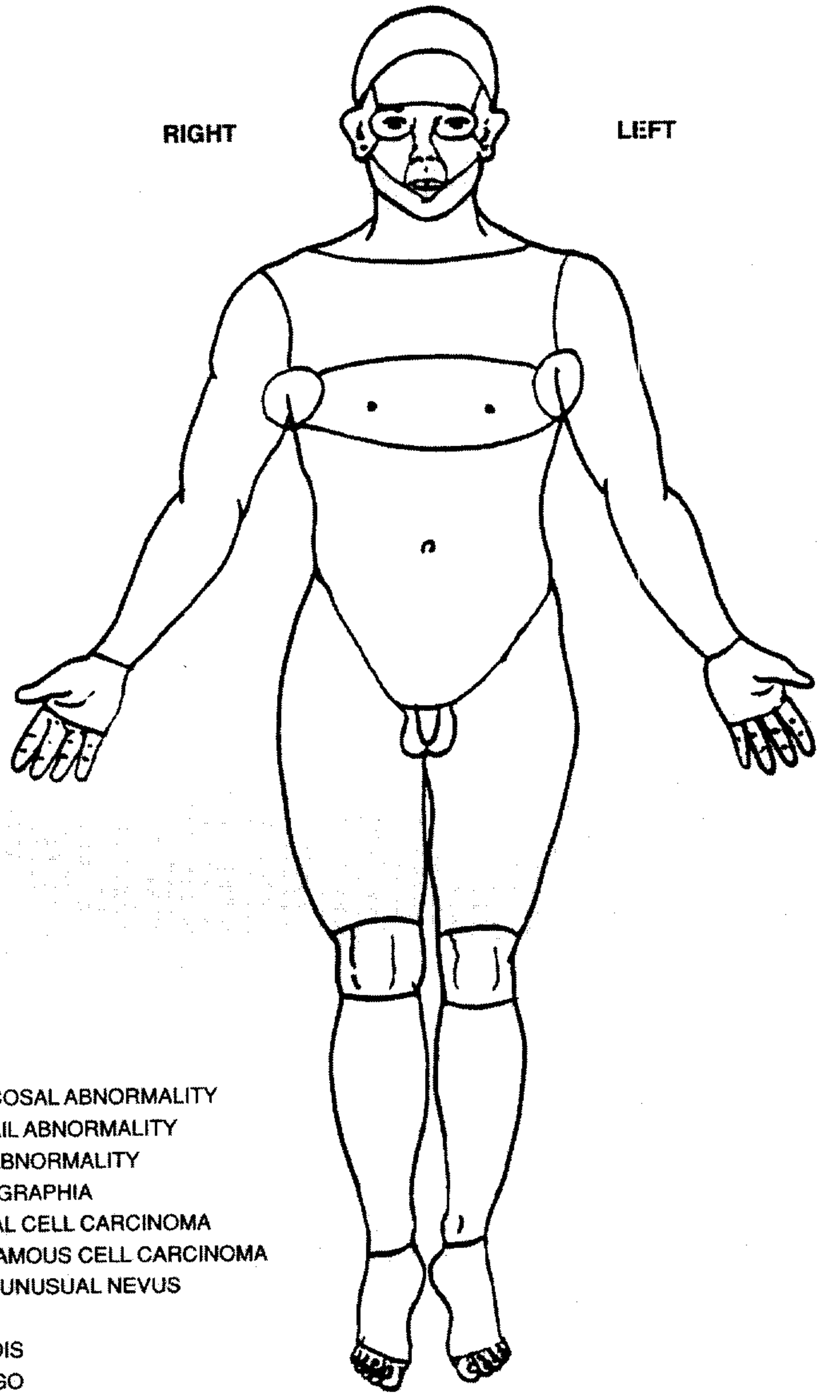
PARTICIPANT LABEL	CASE NUMBER	GROUP NUMBER
	0 1 2 3 4 5 6 7 8 9	0 1 2 3 4 5 6 7 8 9
	0 1 2 3 4 5 6 7 8 9	0 1 2 3 4 5 6 7 8 9
	0 1 2 3 4 5 6 7 8 9	EXAMINER I.D.
	0 1 2 3 4 5 6 7 8 9	0 1 2 3 4 5 6 7 8 9
	0 1 2 3 4 5 6 7 8 9	0 1 2 3 4 5 6 7 8 9
	0 1 2 3 4 5 6 7 8 9	0 1 2 3 4 5 6 7 8 9

FORM AFHS - 9 ANATOMICAL CHART (SHEET 1 0F 2)

YEAR 15 FOLLOW UP

RIGHT





Y N LESION(S) PRESENT ON FRONT

LESION TYPE LEGEND

1 COMEDONES
2 ACNEIFORM LESIONS
3 ACNEIFORM SCARS
4 DEPIGMENTATION
5 INCLUSION CYSTS
6 CUTIS RHOMBOIDALIS
7 HYPERPIGMENTATION
8 JAUNDICE
9 SPIDER ANGIOMATA
10 PALMAR ERYTHEMA
11 SUSPECTED MELANOMA
12 PALMAR KERATOSES
13 ACTINIC KERATOSES
14 PETECHIAE
15 ECCHYMOSES
16 CONJUNCTIVAL ABNORMALITY
17 ORAL MUCOSAL ABNORMALITY
18 FINGERNAIL ABNORMALITY
19 TOENAIL ABNORMALITY
20 DERMATOGRAPHIA
21 SUS. BASAL CELL CARCINOMA
22 SUS. SQUAMOUS CELL CARCINOMA
23 ATYPICAL/UNUSUAL NEVUS
24 VITILIGO
25 TINEA PEDIS
26 INTERTRIGO
27 LIPOMA
28 ECZEMA
29 PSORIASIS
30 SEBORRHEIC DERMATITIS
31 OTHER ABNORMALITY(IES)

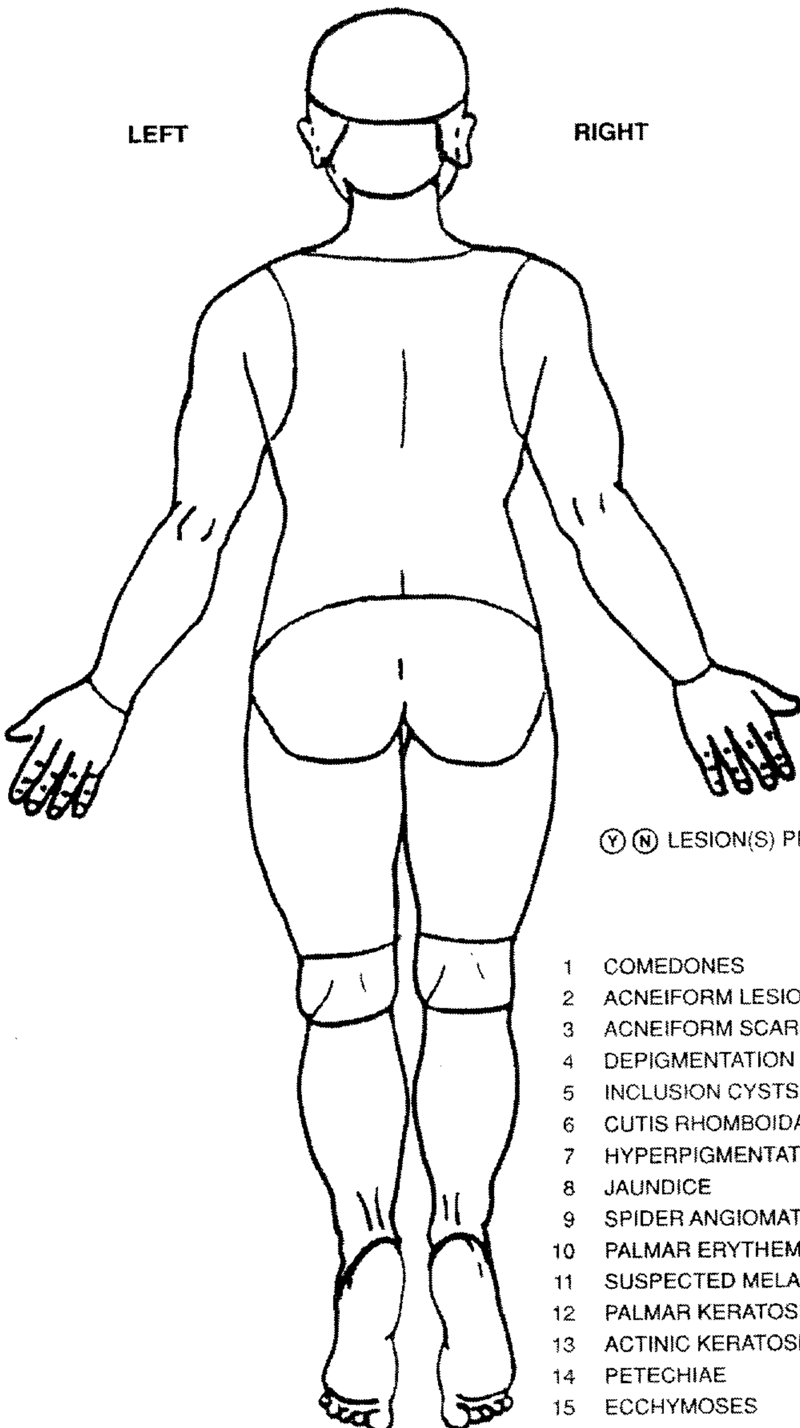
FORM QA AUDIT BY:
1 2 3 4 5 6 INITIALS:
DATE:

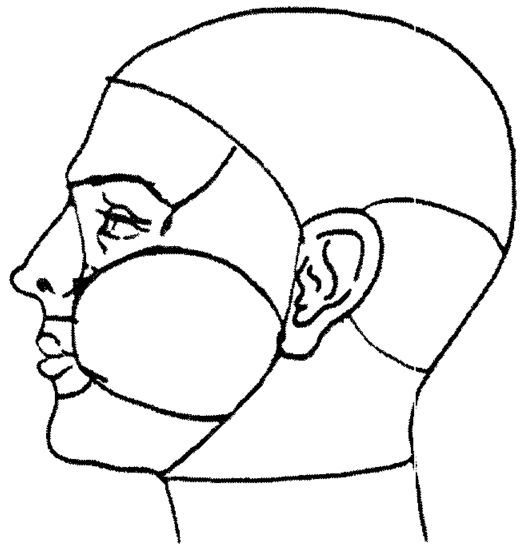
Mark Reflex® by NCS MM212101-1 654321 GS99 Printed in U.S.A.

PARTICIPANT LABEL	CASE NUMBER	GROUP NUMBER
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	EXAMINER I.D.
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨

FORM AFHS - 9 ANATOMICAL CHART (SHEET 2 0F 2)

YEAR 15 FOLLOW UP





Ⓨ Ⓝ LESION(S) PRESENT ON BACK

LESION TYPE LEGEND

1	COMEDONES	17	ORAL MUCOSAL ABNORMALITY
2	ACNEIFORM LESIONS	18	FINGERNAIL ABNORMALITY
3	ACNEIFORM SCARS	19	TOENAIL ABNORMALITY
4	DEPIGMENTATION	20	DERMATOGRAPHIA
5	INCLUSION CYSTS	21	SUS. BASAL CELL CARCINOMA
6	CUTIS RHOMBOIDALIS	22	SUS. SQUAMOUS CELL CARCINOMA
7	HYPERPIGMENTATION	23	ATYPICAL/UNUSUAL NEVUS
8	JAUNDICE	24	VITILIGO
9	SPIDER ANGIOMATA	25	TINEA PEDIS
10	PALMAR ERYTHEMA	26	INTERTRIGO
11	SUSPECTED MELANOMA	27	LIPOMA
12	PALMAR KERATOSES	28	ECZEMA
13	ACTINIC KERATOSES	29	PSORIASIS
14	PETECHIAE	30	SEBORRHEIC DERMATITIS
15	ECCHYMOSES	31	OTHER ABNORMALITY(IES)
16	CONJUNCTIVAL ABNORMALITY		

PRINTED NAME OF EXAMINING PHYSICIAN	SIGNATURE/DATE	FORM QA AUDIT BY: ①②③④⑤⑥	INITIALS:
		DATE:	

PARTICIPANT LABEL	CASE NUMBER	GROUP NUMBER
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	EXAMINER I.D.
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨

UNITED STATES AIR FORCE HEALTH STUDY

FORM AFHS - 10 ELECTROCARDIOGRAM REPORT

YEAR 15 FOLLOW-UP

ECG EXAM WAS/IS:	○ NORMAL	○ ABNORMAL	○ REFUSED
FOLLOW-UP RECOMMENDED?	○ NO	○ YES	
PARTICIPANT COMPLY WITH 4 HOUR ABSTINENCE	○ YES	○ NO	
TECHNICALLY	○ SATISFACTORY	○ UNSATISFACTORY	
RHYTHM: NORMAL SINUS	○ YES	○ NO	

RATE

TACHYCARDIA >100			BRADYCARDIA <50	
⓪	⓪	⓪	⓪	⓪
①	①	①	①	①
②	②	②	②	②
③	③	③	③	③
④	④	④	④	④
⑤	⑤	⑤	⑤	⑤
⑥	⑥	⑥	⑥	⑥
⑦	⑦	⑦	⑦	⑦
⑧	⑧	⑧	⑧	⑧
⑨	⑨	⑨	⑨	⑨

INTERVALS

PR	○ SHORTENED	○ NORMAL	○ PROLONGED	
QRS		○ NORMAL	○ PROLONGED	
	○ RBBB	○ LBBB	○ OIVCD	
QT		○ NORMAL	○ PROLONGED	
AXIS:		○ NORMAL	○ RIGHT	○ LEFT

MORPHOLOGY

P-WAVE:	○ NORMAL	○ ABNORMAL	
QRS	○ NORMAL	○ ABNORMAL	○ OTHER
ST-T	○ NORMAL	○ ABNORMAL	
Q-WAVE	○ NORMAL	○ ABNORMAL	
U-WAVE	○ PRESENT	○ ABSENT	

CHAMBER ENLARGEMENT

RIGHT ATRIAL	Ⓨ	Ⓝ
LEFT ATRIAL	Ⓨ	Ⓝ
RIGHT VENTRIC	Ⓨ	Ⓝ
LEFT VENTRIC	Ⓨ	Ⓝ

PRIOR INFARCTION Ⓨ Ⓝ

- INFERIOR ○
- ANTEROSEPTAL ○
- ANTERIOR ○
- LATERAL ○

ARRHYTHMIA? ○ YES

IF YES
→ RHYTHM STRIP ATTACHED Ⓨ Ⓝ
→ WILL REQUEST PREVIOUS RHYTHM STRIPS Ⓨ Ⓝ
→ **NOTE TYPE**

○ ATRIAL FLUTTER
○ ATRIAL FIBRILLATION
○ A-V DISSOCIATION
○ JUNCTIONAL RHYTHM
○ MULTIFOCAL ATRIAL RHYTHM
○ MULTIFOCAL ○ PVCS ○ PACS
○ UNIFOCAL ○ PVCS ○ PACS
○ OTHER (DESCRIBE IN COMMENTS)

-A-V NODAL Ⓨ Ⓝ

1st° A-V BLOCK ○
2nd° A-V BLOCK ○
3rd° A-V BLOCK ○

OTHER
○ LOW QRS VOLTAGE
○ ANEURYSM ○ INFERIOR ○ ANTERIOR ○ ANTEROSEPTAL ○ LATERAL
○ EARLY REPOLARIZATION
○ PRE EXCITATION ○ WPW ○ LGL ○ OTHER

Ⓨ Ⓝ COMMENTS

TECHNICIANS	ID#	INITIALS
①②③④⑤⑥		

PRINTED NAME OF CARDIOLOGIST/DATE	ID#	INITIALS	FORM QA AUDIT BY:
			①②③④⑤⑥ INITIALS:
			DATE:

PARTICIPANT LABEL	CASE NUMBER	GROUP NUMBER
	⓪①②③④⑤⑥⑦⑧⑨ (×6)	⓪①②③④⑤⑥⑦⑧⑨ (×2)
		EXAMINER I.D.
		⓪①②③④⑤⑥⑦⑧⑨ (×3)

FORM AFHS - 11 RADIOLOGY EXAMINATION

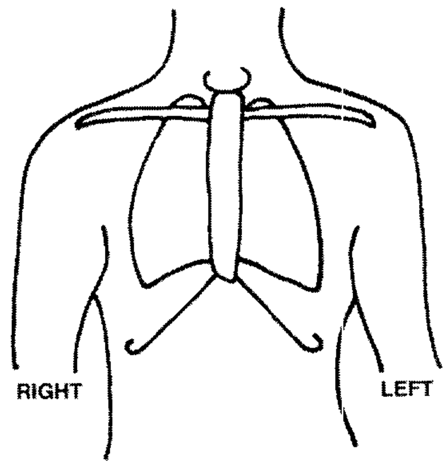
YEAR 15 FOLLOW-UP

CHEST X-RAY EXAM WAS: ○ NORMAL, NO FINDINGS ○ NORMAL WITH FINDINGS ○ ABNORMAL ○ NEED PRIOR FILM(S) ○ REFUSED

FILM QUALITY IS: ○ GOOD ○ FAIR ○ WAS REPEATED

FOLLOW-UP NEEDED: ○ YES ○ NO

COMMENTS/RECOMMENDATIONS: ○ YES ○ NO



ANTERIOR

(PLEASE NOTE THE LOCATIONS IN ABOVE DIAGRAM)

NORMAL **ABNORMAL**

Ⓨ Ⓝ LUNGS
- 1 GRANULOMATUS CHANGES Ⓡ ○ OLD ○ SUSPECT; Ⓛ ○ OLD ○ SUSPECT
- 2 INFILTRATE Ⓡ ○ ACUTE ○ CHRONIC; Ⓛ ○ ACUTE ○ CHRONIC
- 3 HYPERINFLATION Ⓡ ○ COPD ○ OTHER; Ⓛ ○ COPD ○ OTHER
- LESION/NODULE/DENSITY
- 4 Ⓡ ○ BENIGN ○ SUSPECT ○ CALCIFIED; Ⓛ ○ BENIGN ○ SUSPECT ○ CALCIFIED
- 5 Ⓡ Ⓛ INTERSTITIAL MARKINGS
- 6 Ⓡ Ⓛ OTHER

Ⓨ Ⓝ ARTERIAL VASCULATURE
- ○ DILATED/TORTUOUS AORTA ○ ASC ○ DESC ○ ARCH
- ○ AORTIC/TORTUOUS AORTA ○ ASC ○ DESC ○ ARCH
- ○ CALCIFICATIONS ○ ASC ○ DESC ○ ARCH
- ○ OTHER: ○ ASC ○ DESC ○ ARCH
- ○ OTHER

Ⓨ Ⓝ VENOUS VASCULATURE
- ○ A-V MALFORMATION
- ○ PULMONARY VENOUS CONGESTION

Ⓨ Ⓝ DIAPHRAGMS
- ELEVATED Ⓡ Ⓛ
- ○ HIATAL HERNIA
- ○ OTHER

HEART NORMAL Ⓨ Ⓝ
CHAMBER ↑
- Ⓡ Ⓛ ATRIAL
- Ⓡ Ⓛ VENTRICULAR
- Ⓡ Ⓛ OTHER

PLEURA NORMAL Ⓨ Ⓝ RIGHT Ⓨ Ⓝ LEFT
- Ⓨ Ⓝ THICKENED
  - Ⓡ Ⓛ APICAL
  - Ⓡ Ⓛ BASE
  - Ⓡ Ⓛ OTHER

BONEY STRUCTURES NORMAL Ⓨ Ⓝ
COMMENT Ⓨ Ⓝ

RIB ABNORMALITY ○ CERVICAL ○ HYPOPLASTIC ○ FUSED

PRIOR FRACTURES: ○ STERNUM ○ SPINE ○ CLAVICLE ○ RIBS

DEGENERATIVE CHANGES: ○ CERVICAL ○ DORSAL

SPINAL CURVATURE: ○ SCOLIOSIS ○ KYPHOSIS

POST SURGICAL CHANGES
- ○ PRIOR THORACTOMY
- ○ PRIOR CARDIAC SURGERY
- ○ PACEMAKER
- ○ OTHER:

X-RAY TECHNOLOGIST ID# ⓪①②③④⑤⑥⑦⑧⑨ (×2) INITIALS/DATE

FORM QA AUDIT BY: ①②③④⑤⑥ INITIALS:
DATE:

Mark Reflex® by NCS MM212107-1 654321 GS99 Printed in U.S.A.

PARTICIPANT LABEL	CASE NUMBER	GROUP NUMBER
	0 1 2 3 4 5 6 7 8 9	0 1 2 3 4 5 6 7 8 9
	0 1 2 3 4 5 6 7 8 9	0 1 2 3 4 5 6 7 8 9
	0 1 2 3 4 5 6 7 8 9	EXAMINER I.D.
	0 1 2 3 4 5 6 7 8 9	0 1 2 3 4 5 6 7 8 9
	0 1 2 3 4 5 6 7 8 9	0 1 2 3 4 5 6 7 8 9
	0 1 2 3 4 5 6 7 8 9	0 1 2 3 4 5 6 7 8 9

FORM AFHS - 14 VASCULAR LABORATORY - DOPPLER

YEAR 15 FOLLOW UP

yes	no	
Y	N	Are films attached? How many?________________
Y	N	Did participant comply with 4 hour abstinence requirement?

0 = no arterial flow
1 = monophasic arterial flow
2 = biphasic arterial flow
3 = triphasic arterial flow

	R_VASCULAR Right					L_VASCULAR Left				
	cne					cne				
Radial	X	0	1	2	3	X	0	1	2	3
Femoral	X	0	1	2	3	X	0	1	2	3
Popliteal	X	0	1	2	3	X	0	1	2	3
Dorsalis Pedis	X	0	1	2	3	X	0	1	2	3
Posterior Tibial	X	0	1	2	3	X	0	1	2	3

Follow-up: Y N

VASCULAR

Comments/Recommendations: Y N

○ Participant refused

PRINTED NAME OF R.V.T./DATE	ID#	INITIALS	TECHNICIAN ID#	INITIALS	FORM QA AUDIT BY:	
			1 2 3 4 5 6		1 2 3 4 5 6	INITIALS:
					DATE:	

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PARTICIPANT LABEL:

UNITED STATES AIR FORCE HEALTH STUDY

YEAR 15 FOLLOW UP

FORM AFHS - 16A DIAGNOSTIC SUMMARY (MEDICAL)

ICD-9-CM CODE	CHECK ONE: PRE-EXISTING	NEWLY DIAGNOSED	DIAGNOSIS BASED ON PHYSICAL EXAMS; ECG; HEMOCCULT; CHEST X-RAY; SPIROMETRY; VASCULAR; AND LABORATORY STUDIES

HEALTH PROMOTION SUGGESTIONS:	WEIGHT:	SMOKING:	ALCOHOL:

COMMENTS:	FOLLOW-UP NEEDED:	COPIES GIVEN TO PARTICIPANT: YES NO
	1.	1.
	2.	2.
	3.	3.
	4.	4.

RESULTS OF THE EXAMINATION AND RECOMMENDATIONS FOR FOLLOW-UP HAVE BEEN REVIEWED WITH ME.

PARTICIPANT:____________________ DATE:________
SIGNATURE

DIAGNOSTICIAN:________________ ID#:______ DATE:________
SIGNATURE

FORM QA AUDIT DONE BY:
ID# INITIALS DATE

PARTICIPANT LABEL:

DATE OF DIAGNOSIS (MO/DAY/YR):

YEAR 15 FOLLOW UP

FORM AFHS - 16B DIAGNOSTIC SUMMARY (PSYCHOMETRIC)

ICD-9-CM CODE	CHECK ONE: PRE-EXISTING	NEWLY DIAGNOSED	DIAGNOSIS BASED ON PSYCHOLOGICAL TESTING: SCL-90-R

COMMENTS:

PRINTED NAME OF PSYCHOLOGIST:	ID#	INITIALS	DATE	FORM QA AUDIT DONE BY: ID#	INITIALS	DATE

PARTICIPANT LABEL	CASE NUMBER	GROUP NUMBER
	0 1 2 3 4 5 6 7 8 9	0 1 2 3 4 5 6 7 8 9
	0 1 2 3 4 5 6 7 8 9	0 1 2 3 4 5 6 7 8 9
	0 1 2 3 4 5 6 7 8 9	EXAMINER I.D.
	0 1 2 3 4 5 6 7 8 9	0 1 2 3 4 5 6 7 8 9
	0 1 2 3 4 5 6 7 8 9	0 1 2 3 4 5 6 7 8 9
	0 1 2 3 4 5 6 7 8 9	0 1 2 3 4 5 6 7 8 9

FORM AFHS-22 HEMOCCULT EXAMINATION

YEAR 15 FOLLOW UP

PART 1

(TO BE COMPLETED BY PARTICIPANT)

Please record the date of each stool sampled below and describe any alterations from the hemoccult diet. The clinic will complete part 2.

	PACKET 1	PACKET 2	PACKET 3
	MO / DAY / YR	MO / DAY / YR	MO / DAY / YR
Date of smear:			
Comply with diet?	Y N	Y N	Y N

Y N COMMENTS:

PART 2 SKD HEMOCCULT II SLIDE SAMPLE KIT EXAMINATION RESULTS

(TO BE COMPLETED BY THE CLINIC)

	PACKET 1	PACKET 2	PACKET 3
Results:	○ Positive	○ Positive	○ Positive
	○ Negative	○ Negative	○ Negative
	○ No sample	○ No sample	○ No sample

SLIDE SAMPLE KIT WAS:

- ○ Complete (all 3 packets)
- ○ Incomplete (< 3 packets)
- ○ Sampled at rectal exam (0 packets)

HEMOCCULT EXAM WAS:

- ○ All negative
- ○ At least 1 positive

Y N COMMENTS/RECOMMENDATIONS:

PRINTED NAME OF GASTROENTEROLOGIST	ID #	INITIALS	DATE	FORM QA AUDIT BY: 1 2 3 4 5 6	INITIALS:
				DATE:	

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U.S. AIR FORCE HEALTH STUDY - La Jolla, California

GROUP NUMBER
⓪①②③④⑤⑥⑦⑧⑨
⓪①②③④⑤⑥⑦⑧⑨

YEAR 15 FOLLOW-UP

FORM AFHS - 31 EVALUATION

Dear Health Study Participant:

To serve you and future study participants in the best way possible, please complete this short evaluation form. The form may be completed and delivered to the Health Study Logistic Coordinator following your outbriefing at the Scripps Clinic on the second day of your examination.

	excellent	good	satisfactory	unsatisfactory	not applicable
Initial phone contact and recruitment	○	○	○	○	○
Travel agent contact and travel arrangements	○	○	○	○	○
Logistics Information Packet (mailed)	○	○	○	○	○
Airport/Hotel shuttle service	○	○	○	○	○
Hotel/Clinic van service	○	○	○	○	○
Hotel accommodations	○	○	○	○	○
Evening orientation meeting	○	○	○	○	○
Wives orientation meeting	○	○	○	○	○
Cafeteria meals at the Clinic	○	○	○	○	○
Examination schedule at the Clinic	○	○	○	○	○
Technicians (e.g., blood draw)	○	○	○	○	○
Interviews	○	○	○	○	○
Nursing Staff	○	○	○	○	○
Psychological tests	○	○	○	○	○
Examining physicians	○	○	○	○	○
Clinical outbriefing	○	○	○	○	○
Air Force Health Study Monitor	○	○	○	○	○
Overall clinical experience	○	○	○	○	○

Did any examining physician ask about your specific duties in Southeast Asia? ○ yes ○ no
(If yes, please see the Air Force On-site Monitor immediately)

Ⓨ Ⓝ **Additional comments or acknowledgements:** ____________________

____

____

____________________ **Name:** ____________________
(not required)

Mailing Address:

Air Force Health Study M/S C5
Science Applications International Corporation
10260 Campus Point Drive
San Diego, California 92121

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PARTICIPANT LABEL	CASE NUMBER	GROUP NUMBER
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	EXAMINER I.D.
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨

FORM AFHS - 33 CHECKLIST FOR PARTICIPANT FOLDER

YEAR 15 FOLLOW UP

NORC	PIC	3A	3B	4A	4B	5	9	10	11	14	16A	16B	22	32	SCL	JNK	PUL	LAB
Ⓟ	Ⓟ	○	○	○	○	○	○	○ Ⓣ	○ Ⓒ	○ Ⓣ	○	○	○	○	○	○	○	Ⓟ Ⓒ

	DIOX	IMMUNE
BLOOD DRAW INDICATED?	Ⓨ Ⓝ	Ⓨ Ⓝ
DONE?	Ⓨ Ⓝ	Ⓨ Ⓝ

	DX	IM
REFUSED	○	○
RECENT OPERATION	○	○
GAVE BLOOD RECENTLY	○	○
HEMOGLOBIN < 12.5	○	○
SICK (HAD TEMP. ETC)	○	○
OTHER:	○	○

PLEASE SPECIFY OTHER:

DX ______________________________

IM ______________________________

FOLLOW-UP INDICATED? Ⓨ Ⓝ
AUTHORIZATIONS ENCL.? Ⓨ Ⓝ

COPY LETTER ENCLOSED? Ⓨ Ⓝ

CONSENT FORMS ENCLOSED?

PHYS EX/PSYCH Ⓨ Ⓝ
ADIPOSE TISSUE Ⓨ Ⓝ
HIV TEST Ⓨ Ⓝ
SKIN BIOPSY Ⓨ Ⓝ
Ⓨ Ⓝ
Ⓨ Ⓝ

INCIDENT? Ⓨ Ⓝ

MONITOR ID ①②③④⑤⑥

HEMOCCULT SLIDE ENCL? Ⓨ Ⓝ
MEDICAL RECORDS Ⓟ Ⓢ Ⓒ

COMMENTS: Ⓨ Ⓝ

____

____

____

A ○○○○

B ○○○○

C ○○○○

D ○○○○

E ○○○○

LEGEND: P=INDIVID PHOTO ENCLOSED FORM 10: T=ECG TRACINGS ENCLOSED
FORM 11: C=CHEST (X-RAY ENCLOSED)
FORM 14: T=TRACINGS ENCLOSED
LAB: P=PRELIMINARY RESULTS ENCLOSED, C=COMPLETED RESULTS ENCLOSED
MEDICAL RECORDS: P=PARTICIPANT, S=SPOUSE, C=CHILD (ENCLOSED)
DX=DIOXIN IM=IMMUNE

FORM QA AUDIT BY:
①②③④⑤⑥ INITIALS:

DATE:

PARTICIPANT LABEL	CASE NUMBER	GROUP NUMBER
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	EXAMINER I.D.
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨

UNITED STATES AIR FORCE HEALTH STUDY

FORM AFHS - JAS JENKINS ACTIVITY SURVEY

YEAR 15 FOLLOW UP

MARKING INSTRUCTIONS

- Use No. 2 pencil only.
- Do not use ink or felt tip pens.
- Erase cleanly any mark you wish to change.
- Make solid marks that fill the circles completely.
- Make no stray marks on this form.

CORRECT MARK ● USE NO. 2 PENCIL ONLY

INCORRECT MARKS

AGE

⓪	⓪
①	①
②	②
③	③
④	④
⑤	⑤
⑥	⑥
⑦	⑦
⑧	⑧
⑨	⑨

1 Ⓐ Ⓑ Ⓒ	16 Ⓐ Ⓑ Ⓒ Ⓓ	31 Ⓐ Ⓑ Ⓒ	46 Ⓐ Ⓑ Ⓒ Ⓓ
2 Ⓐ Ⓑ Ⓒ	17 Ⓐ Ⓑ Ⓒ Ⓓ	32 Ⓐ Ⓑ Ⓒ	47 Ⓐ Ⓑ Ⓒ
3 Ⓐ Ⓑ Ⓒ Ⓓ	18 Ⓐ Ⓑ Ⓒ Ⓓ	33 Ⓐ Ⓑ Ⓒ	48 Ⓐ Ⓑ Ⓒ
4 Ⓐ Ⓑ Ⓒ Ⓓ Ⓔ	19 Ⓐ Ⓑ Ⓒ	34 Ⓐ Ⓑ	49 Ⓐ Ⓑ Ⓒ
5 Ⓐ Ⓑ	20 Ⓐ Ⓑ Ⓒ Ⓓ	35 Ⓐ Ⓑ Ⓒ	50 Ⓐ Ⓑ Ⓒ Ⓓ Ⓔ
6 Ⓐ Ⓑ Ⓒ Ⓓ	21 Ⓐ Ⓑ Ⓒ Ⓓ	36 Ⓐ Ⓑ Ⓒ	51 Ⓐ Ⓑ Ⓒ Ⓓ Ⓔ Ⓕ Ⓖ Ⓗ
7 Ⓐ Ⓑ Ⓒ	22 Ⓐ Ⓑ Ⓒ Ⓓ	37 Ⓐ Ⓑ Ⓒ	52 Ⓐ Ⓑ Ⓒ
8 Ⓐ Ⓑ Ⓒ	23 Ⓐ Ⓑ Ⓒ Ⓓ	38 Ⓐ Ⓑ Ⓒ Ⓓ	
9 Ⓐ Ⓑ Ⓒ	24 Ⓐ Ⓑ Ⓒ Ⓓ	39 Ⓐ Ⓑ	
10 Ⓐ Ⓑ Ⓒ	25 Ⓐ Ⓑ Ⓒ Ⓓ	40 Ⓐ Ⓑ Ⓒ	
11 Ⓐ Ⓑ Ⓒ	26 Ⓐ Ⓑ Ⓒ Ⓓ	41 Ⓐ Ⓑ Ⓒ	
12 Ⓐ Ⓑ Ⓒ	27 Ⓐ Ⓑ Ⓒ	42 Ⓐ Ⓑ Ⓒ Ⓓ	
13 Ⓐ Ⓑ Ⓒ	28 Ⓐ Ⓑ Ⓒ Ⓓ	43 Ⓐ Ⓑ Ⓒ Ⓓ	
14 Ⓐ Ⓑ Ⓒ Ⓓ	29 Ⓐ Ⓑ Ⓒ	44 Ⓐ Ⓑ Ⓒ Ⓓ	
15 Ⓐ Ⓑ Ⓒ Ⓓ	30 Ⓐ Ⓑ Ⓒ	45 Ⓐ Ⓑ Ⓒ Ⓓ	

FORM QA AUDIT BY:
① ② ③ ④ ⑤ ⑥ INITIALS:
DATE:

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APPENDIX C

APPENDIX C. STUDY SELECTION AND PARTICIPATION

Table C-1. Compliance of Ranch Hands by Examination Year

Time Period	Disposition	Baseline Compliance FC	PC	R	UNL	NS	Total
Baseline		***1,046***	***127***	***34***	***2***	--	***1,209***
1985 Examination	***Eligible***	***1,046***	***127***	***34***	***2***	--	***1,209***
Between Baseline & 1985 Examination	New to Study	--	--	--	--	9	9
	Died	(10)	(9)	(0)	(0)	(0)	(19)
	Remaining Eligible	***1,036***	***118***	***34***	***2***	***9***	***1,199***
	Subject Unlocatable	(27)	(12)	(0)	(0)	(0)	(39)
	Refused	(37)	(67)	(29)	(1)	(0)	(134)
	Partially Compliant	--	--	(5)	(0)	(4)	(9)
	Fully Compliant	***972***	***39***	***0***	***1***	***5***	***1,017***
1987 Examination	***Eligible***	***1,036***	***118***	***34***	***2***	***9***	***1,199***
Between 1985 & 1987 Examination	New to Study	--	--	--	--	4	4
	Died	(12)	(2)	(1)	(0)	(0)	(15)
	Remaining Eligible	***1,024***	***116***	***33***	***2***	***13***	***1,188***
	Subject Unlocatable	(8)	(10)	(2)	(0)	(0)	(20)
	Refused	(71)	(69)	(27)	(1)	(3)	(171)
	Partially Compliant	--	--	(1)	(0)	(0)	(1)
	Fully Compliant	***945***	***37***	***3***	***1***	***10***	***996***
1992 Examination	***Eligible***	***1,024***	***116***	***33***	***2***	***13***	***1,188***
Between 1987 & 1992 Examination	New to Study	--	--	--	--	(0)	(0)
	Died	(35)	(2)	(2)	(0)	(0)	(39)
	Remaining Eligible	***989***	***114***	***31***	***2***	***13***	***1,149***
	Subject Unlocatable	(5)	(4)	(2)	(1)	(0)	(12)
	Refused	(82)	(75)	(23)	(0)	(4)	(184)
	Fully Compliant	***902***	***35***	***6***	***1***	***9***	***953***
1997 Examination	***Eligible***	***989***	***114***	***31***	***2***	***13***	***1,149***
Between 1992 & 1997 Examination	New to Study	--	--	--	--	(0)	(0)
	Died	(40)	(7)	(1)	(0)	(0)	(48)
	Remaining Eligible	***949***	***107***	***30***	***2***	***13***	***1,101***
	Subject Unlocatable	(1)	(0)	(2)	(1)	(0)	(4)
	Refused	(129)	(71)	(23)	(0)	(4)	(227)
	Fully Compliant	***819***	***36***	***5***	***1***	***9***	***870***

FC = Fully Compliant at Baseline
PC = Partially Compliant at Baseline
R = Refusal at Baseline
UNL = Unlocatable at Baseline
NS = New to Study Since Baseline
-- = Undefined Categories

Table C-2. Compliance of Comparisons by Examination Year

Time Period	Disposition	Baseline Compliance					
		FC	PC	R	UNL	NS	Total
Baseline		***1,223***	***301***	***133***	***9***	--	***1,666***
1985 Examination	***Eligible***	***1,223***	***301***	***133***	***9***	--	***1,666***
Between Baseline & 1985 Examination	New to Study	--	--	--	--	73	73
	Died	(16)	(9)	(1)	(0)	(0)	(26)
	Remaining Eligible	***1,207***	***292***	***132***	***9***	***73***	***1,713***
	Subject Unlocatable	(38)	(26)	(0)	(0)	(1)	(65)
	Refused	(31)	(173)	(87)	(5)	(30)	(326)
	Partially Compliant	--	--	(24)	(0)	(6)	(30)
	Fully Compliant	***1,138***	***93***	***21***	***4***	***36***	***1,292***
1987 Examination	***Eligible***	***1,207***	***292***	***132***	***9***	***73***	***1,713***
Between 1985 & 1987 Examination	New to Study	--	--	--	--	33	33
	Died	(14)	(1)	(1)	(0)	(0)	(16)
	Remaining Eligible	***1,193***	***291***	***131***	***9***	***106***	***1,730***
	Subject Unlocatable	(8)	(20)	(9)	(3)	(7)	(47)
	Refused	(73)	(178)	(88)	(3)	(16)	(358)
	Partially Compliant	--	--	(13)	(0)	(14)	(27)
	Fully Compliant	***1,112***	***93***	***21***	***3***	***69***	***1,298***
1992 Examination	***Eligible***	***1,193***	***291***	***131***	***9***	***106***	***1,730***
Between 1987 & 1992 Examination	New to Study	--	--	--	--	83	83
	Died	(37)	(8)	(1)	(0)	(6)	(52)
	Remaining Eligible	***1,156***	***283***	***130***	***9***	***183***	***1,761***
	Subject Unlocatable	(9)	(8)	(7)	(3)	(29)	(56)
	No Health-Match	--	--	--	--	(11)	(11)
	Refused	(85)	(179)	(95)	(3)	(52)	(414)
	Fully Compliant	***1,062***	***96***	***28***	***3***	***91***	***1,280***
1997 Examination	***Eligible***	***1,156***	***283***	***130***	***9***	***183***	***1,761***
Between 1992 & 1997 Examination	New to Study	--	--	--	--	236	236
	No Health-Match in 1992	--	--	--	--	(11)	(11)
	Died	(40)	(9)	(2)	(0)	(16)	(67)
	Remaining Eligible	***1,116***	***274***	***128***	***9***	***392***	***1,919***
	Subject Unlocatable	(4)	(4)	(7)	(2)	(12)	(29)
	No Health-Match	--	--	--	--	(91)	(91)
	Refused	(136)	(176)	(91)	(3)	(142)	(548)
	Fully Compliant	***976***	***94***	***30***	***4***	***147***	***1,251***

FC = Fully Compliant at Baseline
PC = Partially Compliant at Baseline
R = Refusal at Baseline
UNL = Unlocatable at Baseline
NS = New to Study Since Baseline
-- = Undefined Categories

Table C-3. Compliance of Original Comparisons by Examination Year

Time Period	Disposition	Baseline Compliance					
		FC	PC	R	UNL	NS	Total
Baseline		***935***	***216***	***81***	***3***	--	***1,235***
1985 Examination	***Eligible***	***935***	***216***	***81***	***3***	--	***1,235***
Between Baseline &	New to Study	--	--	--	--	17	17
1985 Examination	Died	(11)	(9)	(1)	(0)	(0)	(21)
	Remaining Eligible	***924***	***207***	***80***	***3***	***17***	***1,231***
	Subject Unlocatable	(28)	(19)	(0)	(0)	(1)	(48)
	Refused	(25)	(127)	(62)	(2)	(4)	(220)
	Partially Compliant	--	--	(8)	(0)	(1)	(9)
	Fully Compliant	***871***	***61***	***10***	***1***	***11***	***954***
1987 Examination	***Eligible***	***924***	***207***	***80***	***3***	***17***	***1,231***
Between 1985 &	New to Study	--	--	--	--	4	4
1987 Examination	Died	(12)	(1)	(0)	(0)	(0)	(13)
	Remaining Eligible	***912***	***206***	***80***	***3***	***21***	***1,222***
	Subject Unlocatable	(7)	(12)	(9)	(2)	(1)	(31)
	Refused	(51)	(131)	(53)	(1)	(6)	(242)
	Partially Compliant	--	--	(11)	(0)	(0)	(11)
	Fully Compliant	***854***	***63***	***7***	***0***	***14***	***938***
1992 Examination	***Eligible***	***912***	***206***	***80***	***3***	***21***	***1,222***
Between 1987 &	New to Study	--	--	--	--	2	2
1992 Examination	Died	(25)	(6)	(0)	(0)	(2)	(33)
	Remaining Eligible	***887***	***200***	***80***	***3***	***21***	***1,191***
	Subject Unlocatable	(6)	(4)	(3)	(2)	(0)	(15)
	Refused	(61)	(132)	(64)	(1)	(6)	(264)
	Fully Compliant	***820***	***64***	***13***	***0***	***15***	***912***
1997 Examination	***Eligible***	***887***	***200***	***80***	***3***	***21***	***1,191***
Between 1992 &	New to Study	--	--	--	--	2	2
1997 Examination	Died	(32)	(9)	(1)	(0)	(0)	(42)
	Remaining Eligible	***855***	***191***	***79***	***3***	***23***	***1,151***
	Subject Unlocatable	(3)	(3)	(4)	(0)	(0)	(10)
	Refused	(106)	(125)	(61)	(2)	(8)	(302)
	Fully Compliant	***746***	***63***	***14***	***1***	***15***	***839***

FC = Fully Compliant at Baseline
PC = Partially Compliant at Baseline
R = Refusal at Baseline
UNL = Unlocatable at Baseline
NS = New to Study Since Baseline
-- = Undefined Categories

Table C-4. Compliance of Replacement Comparisons by Examination Year

Time Period	Disposition	Baseline Compliance					
		FC	PC	R	UNL	NS	Total
Baseline		*288*	*85*	*52*	*6*	--	*431*
1985 Examination	***Eligible***	*288*	*85*	*52*	*6*	--	*431*
Between Baseline &	New to Study	--	--	--	--	56	56
1985 Examination	Died	(5)	(0)	(0)	(0)	(0)	(5)
	Remaining Eligible	*283*	*85*	*52*	*6*	*56*	*482*
	Subject Unlocatable	(10)	(7)	(0)	(0)	(0)	(17)
	Refused	(6)	(46)	(25)	(3)	(26)	(106)
	Partially Compliant	--	--	(16)	(0)	(5)	(21)
	Fully Compliant	*267*	*32*	*11*	*3*	*25*	*338*
1987 Examination	***Eligible***	*283*	*85*	*52*	*6*	*56*	*482*
Between 1985 &	New to Study	--	--	--	--	29	29
1987 Examination	Died	(2)	(0)	(1)	(0)	(0)	(3)
	Remaining Eligible	*281*	*85*	*51*	*6*	*85*	*508*
	Subject Unlocatable	(1)	(8)	(0)	(1)	(6)	(16)
	Refused	(22)	(47)	(35)	(2)	(10)	(116)
	Partially Compliant	--	--	(2)	(0)	(14)	(16)
	Fully Compliant	*258*	*30*	*14*	*3*	*55*	*360*
1992 Examination	***Eligible***	*281*	*85*	*51*	*6*	*85*	*508*
Between 1987 &	New to Study	--	--	--	--	81	81
1992 Examination	Died	(12)	(2)	(1)	(0)	(4)	(19)
	Remaining Eligible	*269*	*83*	*50*	*6*	*162*	*570*
	Subject Unlocatable	(3)	(4)	(4)	(1)	(29)	(41)
	No Health-Match	--	--	--	--	(11)	(11)
	Refused	(24)	(47)	(31)	(2)	(46)	(150)
	Fully Compliant	*242*	*32*	*15*	*3*	*76*	*368*
1997 Examination	***Eligible***	*269*	*83*	*50*	*6*	*162*	*570*
Between 1992 &	New to Study	--	--	--	--	234	234
1997 Examination	No Health-Match in 1992	--	--	--	--	(11)	(11)
	Died	(8)	(0)	(1)	(0)	(16)	(25)
	Remaining Eligible	*261*	*83*	*49*	*6*	*369*	*768*
	Subject Unlocatable	(1)	(1)	(3)	(2)	(12)	(19)
	No Health-Match	--	--	--	--	(91)	(91)
	Refused	(30)	(51)	(30)	(1)	(134)	(246)
	Fully Compliant	*230*	*31*	*16*	*3*	*132*	*412*

FC = Fully Compliant at Baseline
PC = Partially Compliant at Baseline
R = Refusal at Baseline
UNL = Unlocatable at Baseline
NS = New to Study Since Baseline
-- = Undefined Categories

APPENDIX D

Appendix D. Coefficients Of Variation For Quality Control

This appendix contains a table of the coefficients of variation (CVs) for each of the 49 laboratory quality control assays. Included in this table are the target CVs and actual CVs. The targets and standard deviations are given for low, medium, and high level controls. A different entry is provided where control lots were changed. The targets and standard deviations for the separate time periods often change, and these changes should be incorporated into any analysis of these data.

Table D-1. Coefficients of Variation for Quality Control—Trilevel Control Data for the 1997 Air Force Health Study

Test (Variable Name) (units)	Time Period	Target			Actual		
		Low	Medium	High	Low	Medium	High
2-hour Postprandial Glucose (AF2HGL) (mg/dl)	5/1/97–end	3.0	1.6	1.5	2.4	1.9	1.8
α-1-Acid Glycoprotein (AFA1AG) (mg/dl)	5/2/97–8/20/97	5.0	4.8	4.8	2.5	2.9	4.4
	8/21/97–end	8.5	7.5	7.6	3.1	3.6	4.7
α-1-Antitrypsin (AFA1AT) (mg/dl)	5/2/97–8/20/97	6.2	4.2	4.5	7.5	3.6	4.7
	8/21/97–end	12.0	9.9	10.1	8.0	4.1	5.7
α-2-Macroglobulin (AFA2MG) (mg/dl)	5/2/97–8/20/97	4.8	4.4	5.0	4.2	3.9	5.2
	8/21/97–end	12.6	10.0	10.0	5.7	5.5	6.1
Albumin (AFALBU) (mg/dl)	5/2/97–8/20/97	4.8	4.4	4.1	3.4	3.1	3.3
	8/21/97–end	7.6	7.5	7.5	4.6	5.1	5.8
Alkaline Phosphatase (ALKA) (U/l)	5/1/97–6/30/97	10.2	4.5	5.1	10.2	4.1	4.9
	7/1/97–end	10.6	4.7	5.4	12.2	5.5	6.0
ALT (ALT) (U/l)	5/1/97–end	4.5	4.5	4.8	3.6	5.5	3.3
Amylase (AMY) (U/l)	5/1/97–end	2.5	1.8	2.2	2.2	1.3	1.1
Apolipoprotein B (AFAPO) (mg/dl)	5/2/97–8/20/97	5.4	5.2	4.9	2.5	2.8	3.0
	8/21/97–end	10.0	9.0	8.6	4.4	4.4	4.3
AST (ASTA) (U/l)	5/1/97–end	7.6	4.3	3.4	7.3	3.7	2.3
C3 Complement (AFC3C) (mg/dl)	5/2/97–8/20/97	8.6	4.8	4.7	9.3	3.6	4.6
	8/21/97–end	9.5	8.9	8.5	7.7	4.7	5.8

Table D-1. Coefficients of Variation for Quality Control—Trilevel Control Data for the 1997 Air Force Health Study (Continued)

Test (Variable Name) (units)	Time Period	Target			Actual		
		Low	Medium	High	Low	Medium	High
C4 Complement (AFC4C) (mg/dl)	5/2/97–8/20/97	4.8	5.0	4.9	3.5	3.4	3.9
	8/21/97–end	10.0	8.7	9.0	4.6	4.6	4.9
Cholesterol (CHOLA) (mg/dl)	5/1/97–end	3.8	3.2	2.7	3.0	2.3	3.3
Creatine Phosphokinase (CPKA) (U/l)	5/1/97–end	6.1	2.6	3.8	4.2	3.0	2.6
Creatinine (CRETA) (mg/dl)	5/1/97–end	5.6	3.4	2.6	6.4	2.7	2.3
Direct Bilirubin (DBILA) (mg/dl)	5/1/97–end	25.0	20.0	11.1	39.8	10.7	5.8
Estradiol (AFESTR) (pg/ml)	5/1/97–end	9.8	10.0	10.0	12.6	8.7	9.2
Free Testosterone (AFTESF) (pg/ml)	5/1/97–end	14.2	14.7	15.0	21.2	14.0	12.2
FSH (AFFSHR) (mIU/ml)	5/1/97–9/15/97	5.2	5.4	5.0	5.1	4.4	4.8
	9/16/97–end	5.0	5.3	4.9	6.0	4.5	4.7
GGT (GGTA) (U/l)	5/1/97–end	6.0	2.4	3.8	5.4	1.9	1.5
Glucose (GLUCA) (mg/dl)	5/1/97–end	3.0	1.6	1.5	2.4	1.8	1.8
Glycated Hemoglobin (α-1-C Hemoglobin) (AFHA1C) (percent)	5/1/97–end	12.7	10.1	8.2	8.9	7.5	7.8
Haptoglobin (AFHAPT) (mg/dl)	5/2/97–8/20/97	4.9	4.6	4.6	2.9	3.4	3.8
	8/21/97–end	7.5	7.0	7.0	3.7	4.0	4.1
HDL Cholesterol (HDLA) (mg/dl)	5/1/97–end	6.3	11.4	3.7	7.6	6.8	5.2

Table D-1. Coefficients of Variation for Quality Control—Trilevel Control Data for the 1997 Air Force Health Study (Continued)

Test (Variable Name) (units)	Time Period	Target			Actual		
		Low	Medium	High	Low	Medium	High
Hematocrit (HCT) (percent)	4/22/97–5/21/97	4.8	2.6	2.8	1.9	1.4	1.1
	5/22/97–6/25/97	5.1	2.6	3.1	1.3	1.1	1.2
	6/26/97–7/21/97	5.1	2.6	2.7	2.0	1.2	2.1
	7/22/97–8/13/97	5.2	2.6	2.8	1.0	1.3	0.9
	8/14/97–9/8/97	5.1	2.6	2.7	1.1	0.9	0.9
	9/9/97–10/8/97	5.0	2.6	2.7	1.3	1.5	1.8
	10/9/97–11/12/97	5.0	2.7	2.8	1.4	1.4	1.5
	11/13/97–12/10/97	5.0	2.6	2.7	1.6	1.0	2.4
	12/11/97–1/14/98	5.0	2.6	2.8	2.3	1.4	1.7
	1/15/98–2/11/98	5.0	2.6	2.8	1.7	1.4	1.0
	2/12/98–3/18/98	5.1	2.6	2.8	2.2	1.7	1.6
	3/19/98–end	5.0	2.6	2.8	1.1	0.9	1.1

Table D-1. Coefficients of Variation for Quality Control—Trilevel Control Data for the 1997 Air Force Health Study (Continued)

Test (Variable Name) (units)	Time Period	Target			Actual		
		Low	Medium	High	Low	Medium	High
Hemoglobin (HGB) (gm/dl)	4/22/97–5/21/97	2.9	1.6	1.8	1.1	1.0	0.9
	5/22/97–6/25/97	2.9	1.6	1.8	0.8	0.7	1.0
	6/26/97–7/21/97	2.9	1.6	1.8	1.8	0.7	1.0
	7/22/97–8/13/97	3.0	1.6	1.8	1.0	0.6	1.3
	8/14/97–9/8/97	2.9	1.6	1.8	0.5	0.5	0.4
	9/9/97–10/8/97	2.9	1.6	1.8	1.0	0.9	1.3
	10/9/97–11/12/97	2.9	1.6	1.8	1.0	0.9	1.4
	11/13/97–12/10/97	2.9	1.6	1.8	0.9	0.7	1.0
	12/11/97–1/14/98	2.9	1.5	1.8	1.1	0.7	0.8
	1/15/98–2/11/98	2.9	1.6	1.8	0.9	0.8	0.9
	2/12/98–3/18/98	2.9	1.6	1.8	1.1	0.8	0.7
	3/19/98–end	2.9	1.6	1.8	1.1	0.5	0.4
IgA (AFIGA) (mg/dl)	5/2/97–8/20/97	4.9	4.0	4.8	2.9	2.5	3.1
	8/21/97–end	7.6	7.0	7.1	3.8	3.5	3.7
IgG (AFIGG) (mg/dl)	5/2/97–8/20/97	4.7	4.5	5.2	2.3	3.2	3.2
	8/21/97–end	8.0	7.1	6.9	2.9	3.4	3.5
IgM (AFIGM) (mg/dl)	5/2/97–8/20/97	4.3	4.6	4.9	3.3	3.1	3.6
	8/21/97–end	10.0	9.1	8.9	4.3	4.0	4.0
Insulin (AFINS) (μIU/ml @ 2 hrs.)	5/1/97–2/4/98	7.1	4.4	4.0	5.1	5.2	5.6
	2/5/98–end	7.7	7.4	5.3	6.6	8.3	6.7
LDH (LDHA) (U/l)	5/1/97–end	4.5	3.0	3.3	3.6	3.0	2.7
Luteinizing Hormone (AFLH) (mIU/ml)	5/1/97–end	5.0	4.9	4.9	6.0	5.1	6.1

Table D-1. Coefficients of Variation for Quality Control—Trilevel Control Data for the 1997 Air Force Health Study (Continued)

Test (Variable Name) (units)	Time Period	Target			Actual		
		Low	Medium	High	Low	Medium	High
Mean Corpuscular Hemoglobin (MCH) (pg)	4/22/97–5/21/97	2.8	2.0	2.4	1.1	1.0	0.7
	5/22/97–6/25/97	2.8	2.0	2.4	0.9	1.1	1.0
	6/26/97–7/21/97	2.8	2.0	2.4	1.0	0.9	0.8
	7/22/97–8/13/97	2.9	2.0	2.4	1.4	1.3	1.3
	8/14/97–9/8/97	2.8	2.0	2.4	1.1	0.6	0.6
	9/9/97–10/8/97	2.8	2.0	2.4	1.2	0.8	0.9
	10/9/97–11/12/97	2.8	2.0	2.4	1.3	1.0	1.0
	11/13/97–12/10/97	2.8	2.0	2.4	1.5	0.8	1.1
	12/11/97–1/14/98	2.8	2.0	2.4	1.6	1.3	0.9
	1/15/98–2/11/98	2.8	2.0	2.4	1.3	1.1	1.0
	2/12/98–3/18/98	2.8	2.0	2.4	1.3	1.2	1.1
	3/19/98–end	2.9	2.0	2.4	1.0	0.8	0.9

Table D-1. Coefficients of Variation for Quality Control—Trilevel Control Data for the 1997 Air Force Health Study (Continued)

Test (Variable Name) (units)	Time Period	Target			Actual		
		Low	Medium	High	Low	Medium	High
Mean Corpuscular Hemoglobin Concentration (MCHC) (gm/dl)	4/22/97–5/21/97	2.5	3.8	3.1	1.1	1.5	0.6
	5/22/97–6/25/97	2.5	3.9	3.2	1.3	1.7	1.5
	6/26/97–7/21/97	2.5	3.8	3.1	1.4	0.9	0.9
	7/22/97–8/13/97	2.5	4.0	3.2	1.2	1.2	1.0
	8/14/97–9/8/97	2.5	3.9	3.2	0.9	1.3	0.8
	9/9/97–10/8/97	2.5	3.9	3.1	1.1	1.2	1.0
	10/9/97–11/12/97	2.5	3.9	3.1	0.9	1.2	1.0
	11/13/97–12/10/97	2.5	3.9	3.1	1.7	1.8	1.3
	12/11/97–1/14/98	2.5	3.9	3.1	2.0	2.4	1.4
	1/15/98–2/11/98	2.5	3.9	3.1	1.5	1.8	1.3
	2/12/98–3/18/98	2.5	3.8	3.1	1.8	1.7	2.0
	3/19/98–end	2.5	3.9	3.1	1.1	1.0	1.1

Table D-1. Coefficients of Variation for Quality Control—Trilevel Control Data for the 1997 Air Force Health Study (Continued)

Test (Variable Name) (units)	Time Period	Target			Actual		
		Low	Medium	High	Low	Medium	High
Mean Corpuscular Volume (MCV) (cu. micra)	4/22/97–5/21/97	1.8	1.7	1.7	0.8	0.6	0.7
	5/22/97–6/25/97	1.8	1.7	1.7	1.4	0.8	0.5
	6/26/97–7/21/97	1.8	1.7	1.7	0.9	0.9	1.4
	7/22/97–8/13/97	1.9	1.7	1.7	0.9	1.1	1.0
	8/14/97–9/8/97	1.8	1.7	1.7	0.5	0.5	0.5
	9/9/97–10/8/97	1.8	1.7	1.7	0.7	0.6	0.6
	10/9/97–11/12/97	1.8	1.7	1.7	0.7	0.7	0.7
	11/13/97–12/10/97	1.8	1.7	1.7	1.0	0.7	1.2
	12/11/97–1/14/98	1.8	1.7	1.7	1.2	0.9	0.7
	1/15/98–2/11/98	1.8	1.7	1.7	0.7	0.8	0.7
	2/12/98–3/18/98	1.8	1.7	1.7	1.8	1.3	0.8
	3/19/98–end	1.9	1.7	1.7	0.5	0.3	0.6

Table D-1. Coefficients of Variation for Quality Control—Trilevel Control Data for the 1997 Air Force Health Study (Continued)

Test (Variable Name) (units)	Time Period	Target			Actual		
		Low	Medium	High	Low	Medium	High
Platelet Count (PLT) (thousand/mm^3)	4/22/97–5/21/97	10.1	5.5	4.5	4.8	4.5	2.7
	5/22/97–6/25/97	9.4	5.1	4.3	3.0	2.3	3.3
	6/26/97–7/21/97	9.7	5.2	4.5	2.5	2.7	2.0
	7/22/97–8/13/97	9.4	5.0	4.4	3.2	2.2	2.1
	8/14/97–9/8/97	9.4	5.0	4.5	1.8	1.8	1.6
	9/9/97–10/8/97	9.1	5.0	4.4	2.2	1.8	1.8
	10/9/97–11/12/97	9.1	5.1	4.5	4.5	2.6	2.1
	11/13/97–12/10/97	10.1	5.4	4.6	2.2	2.5	2.8
	12/11/97–1/14/98	9.7	5.3	4.6	2.1	2.0	2.2
	1/15/98–2/11/98	10.0	5.4	4.6	2.7	3.5	2.0
	2/12/98–3/18/98	10.3	5.7	4.8	3.3	2.8	2.6
	3/19/98–end	9.9	5.4	4.7	2.1	1.9	2.4
Prealbumin (AFPRAL) (mg/dl)	5/2/97–8/20/97	4.9	4.5	5.0	2.7	3.2	5.4
	8/21/97–end	7.5	7.1	8.0	3.2	3.7	6.4
Prostate Specific Antigen (AFPSA) (ng/ml)	4/30/97–8/10/97	13.2	9.9	10.0	5.6	6.2	6.3
	8/11/97–11/17/97	5.4	5.6	4.4	7.3	5.8	7.1
	11/18/97–2/11/98	5.7	7.0	10.3	5.3	5.5	7.4
	2/12/98–end	5.1	3.8	4.5	4.2	4.5	5.8
Prothrombin Time (AFPTP) (seconds)	5/1/97–end	2.5	2.9	5.0	1.9	2.0	2.2

Table D-1. Coefficients of Variation for Quality Control—Trilevel Control Data for the 1997 Air Force Health Study (Continued)

Test (Variable Name) (units)	Time Period	Target			Actual		
		Low	Medium	High	Low	Medium	High
Red Blood Cell Count (RBC) (million/mm^3)	4/22/97–5/21/97	2.2	1.5	1.6	1.5	0.9	1.0
	5/22/97–6/25/97	2.2	1.5	1.6	1.0	0.7	1.1
	6/26/97–7/21/97	2.2	1.5	1.6	1.3	0.8	1.1
	7/22/97–8/13/97	2.2	1.5	1.7	0.9	1.7	1.0
	8/14/97–9/8/97	2.2	1.5	1.6	0.8	0.6	0.6
	9/9/97–10/8/97	2.2	1.5	1.6	1.0	1.5	1.5
	10/9/97–11/12/97	2.2	1.5	1.7	1.4	1.4	1.3
	11/13/97–12/10/97	2.2	1.5	1.6	1.5	1.0	1.5
	12/11/97–1/14/98	2.2	1.4	1.6	1.7	0.7	1.1
	1/15/98–2/11/98	2.2	1.5	1.6	1.2	0.8	0.7
	2/12/98–3/18/98	2.2	1.5	1.6	1.1	0.9	1.0
	3/19/98–end	2.2	1.5	1.6	1.0	0.7	0.8
Rheumatoid Factor (AFLATX) (IU/ml)	5/1/97–end	50.0	5.0	5.0	0.0	3.6	3.5
T_4 (AFT4) (μg/dl)	5/1/97–10/5/97	7.8	7.8	7.7	7.8	5.6	5.0
	10/6/97–end	7.8	7.8	7.7	11.4	6.5	6.3
Total Bilirubin (TBILA) (mg/dl)	5/1/97–end	15.7	5.8	5.1	8.0	2.8	3.2
Total Testosterone (AFTEST) (ng/dl)	5/1/97–12/3/97	10.4	9.8	4.2	11.5	9.5	7.0
	12/4/97–end	8.2	8.2	7.4	9.0	7.2	6.8
Transferrin (AFTRFR) (mg/dl)	5/2/97–8/26/97	4.6	4.7	4.6	4.6	2.8	3.8
	8/27/97–end	7.6	6.9	7.0	3.8	4.1	5.8
Triglycerides (TRIGA) (mg/dl)	5/1/97–end	16.1	3.7	3.8	15.3	2.9	3.0

Table D-1. Coefficients of Variation for Quality Control—Trilevel Control Data for the 1997 Air Force Health Study (Continued)

Test (Variable Name) (units)	Time Period	Target Low	Target Medium	Target High	Actual Low	Actual Medium	Actual High
TSH (AFTSH) (μIU/ml)	5/1/97–2/14/98	10.0	8.4	8.3	10.1	9.9	11.2
	2/15/98–end	10.0	7.6	7.8	6.1	5.8	5.9
Urinary pH (UAPH)	4/97–end	8.3	6.7	6.3	2.5	3.2	1.2
White Blood Cell Count (WBC) (thousand/mm^3)	4/22/97–5/21/97	5.7	3.8	2.9	2.8	2.4	1.0
	5/22/97–6/25/97	5.9	4.0	2.8	2.4	3.7	0.9
	6/26/97–7/21/97	5.7	3.8	2.8	2.9	1.6	2.3
	7/22/97–8/13/97	5.6	3.8	2.9	2.7	2.4	1.5
	8/14/97–9/8/97	5.7	3.9	2.8	2.5	1.8	0.6
	9/9/97–10/8/97	5.4	3.8	2.8	2.7	2.0	1.3
	10/9/97–11/12/97	5.4	3.9	2.8	2.6	2.6	1.4
	11/13/97–12/10/97	5.4	3.9	2.7	2.3	2.2	1.1
	12/11/97–1/14/98	5.6	4.0	2.8	3.4	2.0	1.0
	1/15/98–2/11/98	5.9	4.0	2.8	2.9	2.8	1.3
	2/12/98–3/18/98	5.7	3.9	2.8	3.6	1.9	1.2
	3/19/98–end	5.6	3.8	2.8	1.6	1.1	0.9

Appendix E

APPENDIX E. STATISTICAL METHODS

Table E-1. Approximate Power To Detect an Initial Dioxin Effect at a 5-Percent Level of Significance (Discrete Dependent Variable)

Prevalence of Condition	Relative Risk 1.10	1.20	1.30	1.40	1.50	1.75	2.00	10.00	20.00
0.005	0.05	0.07	0.09	0.13	0.18	0.35	0.56	1.00	1.00
0.01	0.06	0.09	0.14	0.21	0.30	0.59	0.82	1.00	1.00
0.02	0.07	0.13	0.23	0.36	0.52	0.84	0.97	1.00	1.00
0.03	0.08	0.16	0.31	0.49	0.67	0.94	0.99	1.00	1.00
0.04	0.09	0.20	0.39	0.60	0.78	0.98	1.00	1.00	1.00
0.05	0.10	0.24	0.46	0.68	0.85	0.99	1.00	1.00	1.00
0.10	0.14	0.39	0.70	0.90	0.98	1.00	1.00	1.00	1.00
0.15	0.17	0.51	0.82	0.96	0.99	1.00	1.00	1.00	1.00
0.20	0.20	0.59	0.89	0.98	1.00	1.00	1.00	1.00	1.00

Table E-2. Approximate Power To Detect a Categorized Dioxin Effect (Low plus High Ranch Hands vs. Comparisons) at a 5-Percent Level of Significance (Discrete Dependent Variable)

Prevalence of Condition	Relative Risk 1.10	1.20	1.30	1.40	1.50	1.75	2.00	10.00	20.00
0.005	0.05	0.06	0.07	0.08	0.09	0.13	0.18	0.95	0.99
0.01	0.05	0.06	0.08	0.10	0.13	0.21	0.30	1.00	1.00
0.02	0.06	0.08	0.11	0.15	0.21	0.36	0.53	1.00	1.00
0.03	0.06	0.09	0.14	0.21	0.28	0.50	0.69	1.00	1.00
0.04	0.06	0.11	0.17	0.26	0.35	0.61	0.81	1.00	1.00
0.05	0.07	0.12	0.20	0.30	0.42	0.70	0.88	1.00	1.00
0.10	0.08	0.18	0.33	0.51	0.67	0.92	0.99	1.00	1.00
0.15	0.10	0.24	0.44	0.65	0.81	0.98	1.00	1.00	1.00
0.20	0.11	0.28	0.52	0.74	0.88	0.99	1.00	1.00	1.00

Table E-3. Approximate Power To Detect a Lipid-adjusted 1987 Dioxin Effect at a 5-Percent Level of Significance (Discrete Dependent Variable)

Prevalence of Condition	Relative Risk								
	1.10	1.20	1.30	1.40	1.50	1.75	2.00	10.00	20.00
0.005	0.06	0.09	0.15	0.23	0.34	0.65	0.89	1.00	1.00
0.01	0.07	0.14	0.25	0.40	0.57	0.90	0.99	1.00	1.00
0.02	0.09	0.22	0.43	0.66	0.84	0.99	1.00	1.00	1.00
0.03	0.11	0.30	0.58	0.82	0.95	1.00	1.00	1.00	1.00
0.04	0.13	0.38	0.69	0.90	0.98	1.00	1.00	1.00	1.00
0.05	0.15	0.45	0.78	0.95	0.99	1.00	1.00	1.00	1.00
0.10	0.25	0.70	0.95	1.00	1.00	1.00	1.00	1.00	1.00
0.15	0.32	0.83	0.99	1.00	1.00	1.00	1.00	1.00	1.00
0.20	0.39	0.90	1.00	1.00	1.00	1.00	1.00	1.00	1.00

Table E-4. Approximate Power To Detect an Initial Dioxin Effect at a 5-Percent Level of Significance (Continuous Dependent Variable)

Mean Change	Coefficient of Variation (100 σ/μ)					
	5	10	15	25	50	75
0.005	0.82	0.30	0.16	0.09	0.06	0.05
0.01	1.00	0.82	0.49	0.21	0.09	0.07
0.02	1.00	1.00	0.97	0.64	0.21	0.12
0.03	1.00	1.00	1.00	0.93	0.41	0.21
0.04	1.00	1.00	1.00	1.00	0.64	0.34
0.05	1.00	1.00	1.00	1.00	0.82	0.49
0.10	1.00	1.00	1.00	1.00	1.00	0.97

Table E-5. Approximate Power To Detect a Categorized Dioxin Effect (Low plus High Ranch Hands vs. Comparisons) at a 5-Percent Level of Significance (Continuous Dependent Variable)

	Coefficient of Variation (100 σ/μ)					
Mean Change	**5**	**10**	**15**	**25**	**50**	**75**
0.005	0.46	0.15	0.09	0.07	0.05	0.05
0.01	0.96	0.46	0.24	0.12	0.07	0.06
0.02	1.00	0.96	0.70	0.32	0.12	0.08
0.03	1.00	1.00	0.96	0.61	0.20	0.12
0.04	1.00	1.00	1.00	0.84	0.32	0.17
0.05	1.00	1.00	1.00	0.96	0.46	0.24
0.10	1.00	1.00	1.00	1.00	0.96	0.70

Table E-6. Approximate Power To Detect a Lipid-adjusted 1987 Dioxin Effect at a 5-Percent Level of Significance (Continuous Dependent Variable)

	Coefficient of Variation (100 σ/μ)					
Mean Change	**5**	**10**	**15**	**25**	**50**	**75**
0.005	0.99	0.58	0.30	0.14	0.07	0.06
0.01	1.00	0.99	0.82	0.41	0.14	0.09
0.02	1.00	1.00	1.00	0.93	0.41	0.21
0.03	1.00	1.00	1.00	1.00	0.74	0.41
0.04	1.00	1.00	1.00	1.00	0.93	0.63
0.05	1.00	1.00	1.00	1.00	0.99	0.82
0.10	1.00	1.00	1.00	1.00	1.00	1.00

APPENDIX F

List of Tables

APPENDIX F. DEPENDENT VARIABLE-COVARIATE ASSOCIATIONS

This appendix contains results of tests of association between each dependent variable and covariates for the adjusted analysis of each dependent variable. Pearson's chi-square test (continuity-adjusted for 2x2 tables) is used for significance testing of the associations between each discrete dependent variable and the covariate. When a covariate is continuous in nature (for example, age), the covariate is discretized prior to the analysis of the discrete dependent variable. Pearson's correlation coefficient is used for significance testing of the associations between each continuous dependent variable and a continuous candidate covariate. When a covariate is discrete in nature, means (transformed back to the original scale, if necessary) are presented and an analysis of variance is used to investigate the difference between the means.

Table F-1. Dependent Variable-Covariate Associations for the General Health Assessment

Dependent Variable	Level	Age			Race		
		Born ≥1942	Born <1942	p-Value	Black	Non-Black	p-Value
Self-perception of Health	Fair or Poor	(n=932) 10.7%	(n=1,188) 13.0%	0.132	(n=128) 19.5%	(n=1,992) 11.5%	0.010
Appearance of Illness or Distress	Yes	(n=933) 1.0%	(n=1,188) 1.7%	0.220	(n=128) 4.7%	(n=1,993) 1.2%	0.003
Relative Age Appearance	Older	(n=933) 7.8%	(n=1,188) 10.2%	0.072	(n=128) 7.0%	(n=1,993) 9.3%	0.485
Body Fat		(n=933)	(n=1,188)		(n=128)	(n=1,993)	
(continuous)[a]		r =–0.011		0.621	$\bar{x}$ =22.59	$\bar{x}$ =22.18	0.410
(discrete)	Obese	30.2%	28.5%	0.399	35.2%	28.9%	0.156
Erythrocyte Sedimentation Rate		(n=933)	(n=1,188)		(n=128)	(n=1,993)	
(continuous)[b]		r=0.179		<0.001	$\bar{x}$ =5.33	$\bar{x}$ =4.74	0.184
(discrete)	Abnormal	6.1%	8.7%	0.033	10.2%	7.4%	0.326

Dependent Variable	Level	Occupation				Personality Type		
		Officer	Enlisted Flyer	Enlisted Groundcrew	p-Value	Type A	Type B	p-Value
Self-perception of Health	Fair or Poor	(n=835) 7.7%	(n=338) 14.5%	(n=947) 14.9%	0.001	(n=819) 11.4%	(n=1,298) 12.4%	0.513
Appearance of Illness or Distress	Yes	(n=835) 0.8%	(n=338) 1.5%	(n=948) 1.8%	0.219	--	--	--
Relative Age Appearance	Older	(n=835) 5.6%	(n=338) 12.7%	(n=948) 11.0%	0.001	--	--	--
Body Fat		(n=835)	(n=338)	(n=948)				
(continuous)		$\bar{x}$ =21.94	$\bar{x}$ =21.97	$\bar{x}$ =22.52	0.059	--	--	--
(discrete)	Obese	25.3%	28.1%	33.1%	0.001	--	--	--
Erythrocyte Sedimentation Rate		(n=835)	(n=338)	(n=948)		(n=820)	(n=1,298)	
(continuous)		$\bar{x}$ =4.39	$\bar{x}$ =5.61	$\bar{x}$ =4.85	<0.001	$\bar{x}$ =4.56	$\bar{x}$ =4.91	0.090
(discrete)	Abnormal	6.5%	9.2%	7.9%	0.240	6.3%	8.3%	0.111

Table F-1. Dependent Variable-Covariate Associations for the General Health Assessment (Continued)

Dependent Variable	Level	Current Cigarette Smoking (cigarettes/day)				p-Value
		0-Never	0-Former	>0–20	>20	
Self-perception of Health	Fair or Poor	(n=595) 7.7%	(n=1,116) 11.9%	(n=272) 19.9%	(n=137) 15.3%	0.001
Appearance of Illness or Distress	Yes	(n=595) 0.5%	(n=1,116) 1.3%	(n=272) 2.9%	(n=137) 2.2%	0.030
Relative Age Appearance	Older	(n=595) 3.9%	(n=1,116) 6.5%	(n=272) 23.2%	(n=137) 25.6%	0.001
Body Fat		(n=595)	(n=1,116)	(n=272)	(n=137)	
(continuous)[a]			r=–0.187			<0.001
(discrete)	Obese	27.1%	33.6%	21.3%	19.0%	0.001
Erythrocyte Sedimentation Rate		(n=595)	(n=1,116)	(n=272)	(n=137)	
(continuous)[b]			r=0.021			0.330
(discrete)	Abnormal	4.7%	7.9%	9.9%	12.4%	0.003

Dependent Variable	Level	Lifetime Cigarette Smoking History (pack-years)			p-Value
		0	>0–10	>10	
Self-perception of Health	Fair or Poor	(n=595) 7.7%	(n=558) 10.8%	(n=965) 15.2%	0.001
Appearance of Illness or Distress	Yes	(n=595) 0.5%	(n=558) 1.1%	(n=965) 2.1%	0.027
Relative Age Appearance	Older	(n=595) 3.9%	(n=558) 7.7%	(n=965) 13.2%	0.001
Body Fat		(n=595)	(n=558)	(n=965)	
(continuous)[a]			r=–0.018		0.399
(discrete)	Obese	27.1%	33.7%	28.1%	0.026
Erythrocyte Sedimentation Rate		(n=595)	(n=558)	(n=965)	
(continuous)[b]			r=0.155		<0.001
(discrete)	Abnormal	4.7%	7.2%	9.5%	0.002

Table F-1. Dependent Variable-Covariate Associations for the General Health Assessment (Continued)

Dependent Variable	Level	Current Alcohol Use (drinks/day) 0–1	>1–4	>4	p-Value
Self-perception of Health	Fair or Poor	(n=1,699) 11.7%	(n=371) 13.5%	(n=50) 10.0%	0.580
Appearance of Illness or Distress	Yes	(n=1,699) 1.7%	(n=371) 0.3%	(n=50) 0.0%	0.082
Relative Age Appearance	Older	(n=1,699) 8.7%	(n=371) 11.6%	(n=50) 6.0%	0.161
Body Fat		(n=1,699)	(n=371)	(n=50)	
(continuous)[a]			r=–0.094		<0.001
(discrete)	Obese	30.9%	22.6%	22.0%	0.003
Erythrocyte Sedimentation Rate		(n=1,699)	(n=371)	(n=50)	0.217
(continuous)[b]			r=–0.027		
(discrete)	Abnormal	7.5%	8.4%	4.0%	0.532

Dependent Variable	Level	Lifetime Alcohol History (drink-years) 0	>0–40	>40	p-Value
Self-perception of Health	Fair or Poor	(n=118) 15.3%	(n=1,379) 11.2%	(n=616) 13.3%	0.214
Appearance of Illness or Distress	Yes	(n=118) 0.9%	(n=1,379) 1.1%	(n=616) 2.1%	0.170
Relative Age Appearance	Older	(n=118) 7.6%	(n=1,379) 8.4%	(n=616) 11.2%	0.114
Body Fat		(n=118)	(n=1,379)	(n=616)	
(continuous)[a]			r=–0.050		0.022
(discrete)	Obese	25.4%	29.5%	29.4%	0.642
Erythrocyte Sedimentation Rate		(n=118)	(n=1,379)	(n=616)	0.019
(continuous)[b]			r=0.051		
(discrete)	Abnormal	6.8%	6.7%	9.4%	0.107

[a] Analysis performed on natural logarithm scale; means transformed from natural logarithm scale.

[b] Analysis performed on natural logarithm scale of sedimentation rate + 0.1; means transformed from natural logarithm scale of sedimentation rate + 0.1.

--: Covariate not applicable for dependent variable.

Note: Correlations (r) are based on total sample size and are not category-specific.

Table F-2. Dependent Variable-Covariate Associations for the Neoplasia Assessment

Dependent Variable	Level	Age			Race		
		Born ≥1942	Born <1942	p-Value	Black	Non-Black	p-Value
Any Skin Neoplasm		(n=855)	(n=1,118)				
	Yes	31.5%	41.0%	<0.001	--	--	--
Malignant Skin Neoplasm		(n=855)	(n=1,118)				
	Yes	10.9%	21.3%	<0.001	--	--	--
Benign Skin Neoplasm		(n=927)	(n=1,173)				
	Yes	22.6%	23.9%	0.509	--	--	--
Skin Neoplasm of Uncertain Behavior or Unspecified Nature		(n=855)	(n=1,118)				
	Yes	0.7%	0.8%	0.999	--	--	--
Any Basal Cell Carcinoma		(n=855)	(n=1,118)				
	Yes	8.8%	18.0%	<0.001	--	--	--
Basal Cell Carcinoma on Ear, Face, Head, or Neck		(n=855)	(n=1,118)				
	Yes	5.5%	14.9%	<0.001	--	--	--
Basal Cell Carcinoma on Trunk		(n=855)	(n=1,118)				
	Yes	2.9%	5.6%	0.007	--	--	--
Basal Cell Carcinoma on Upper Extremities		(n=855)	(n=1,118)				
	Yes	2.0%	3.8%	0.031	--	--	--
Basal Cell Carcinoma on Lower Extremities		(n=855)	(n=1,118)				
	Yes	0.4%	0.6%	0.594	--	--	--
Squamous Cell Carcinoma		(n=855)	(n=1,118)				
	Yes	0.9%	3.0%	0.002	--	--	--
Nonmelanoma		(n=855)	(n=1,118)				
	Yes	9.7%	20.3%	<0.001	--	--	--
Melanoma		(n=855)	(n=1,118)				
	Yes	1.2%	1.7%	0.435	--	--	--
Any Systemic Neoplasm		(n=927)	(n=1,170)		(n=127)	(n=1,970)	
	Yes	21.8%	37.2%	<0.001	24.4%	30.8%	0.159
Malignant Systemic Neoplasm		(n=931)	(n=1,179)		(n=127)	(n=1,983)	
	Yes	2.4%	10.2%	<0.001	6.3%	6.8%	0.986
Benign Systemic Neoplasm		(n=927)	(n=1,170)		(n=127)	(n=1,970)	
	Yes	19.2%	28.9%	<0.001	18.9%	25.0%	0.151
Systemic Neoplasm of Uncertain Behavior or Unspecified Nature		(n=931)	(n=1,179)		(n=127)	(n=1,983)	
	Yes	1.4%	2.4%	0.145	1.6%	2.0%	0.999
Malignant Systemic Neoplasm on Eye, Ear, Face, Head, or Neck		(n=931)	(n=1,179)		(n=127)	(n=1,983)	
	Yes	0.4%	1.4%	0.035	0.8%	1.0%	0.999
Malignant Systemic Neoplasm of Oral Cavity, Pharynx, or Larynx		(n=931)	(n=1,179)		(n=127)	(n=1,983)	
	Yes	0.1%	0.9%	0.041	0.8%	0.5%	0.999
Malignant Systemic Neoplasm of Thymus, Heart, or Mediastinum		(n=931)	(n=1,179)		(n=127)	(n=1,983)	
	Yes	0.2%	0.0%	0.379	0.0%	0.1%	0.999
Malignant Systemic Neoplasm of Thyroid Gland		(n=931)	(n=1,179)		(n=127)	(n=1,983)	
	Yes	0.0%	0.3%	0.202	0.0%	0.2%	0.999
Malignant Systemic Neoplasm of Bronchus or Lung		(n=931)	(n=1,179)		(n=127)	(n=1,983)	
	Yes	0.2%	0.9%	0.070	0.0%	0.7%	0.741

Table F-2. Dependent Variable-Covariate Associations for the Neoplasia Assessment (Continued)

		Age			Race		
Dependent Variable	**Level**	**Born ≥1942**	**Born <1942**	**p-Value**	**Black**	**Non-Black**	**p-Value**
Malignant Systemic Neoplasm		(n=931)	(n=1,179)		(n=127)	(n=1,983)	
of Liver	Yes	0.2%	0.2%	0.999	0.0%	0.2%	0.999
Malignant Systemic Neoplasm		(n=931)	(n=1,179)		(n=127)	(n=1,983)	
of Colon or Rectum	Yes	0.6%	0.8%	0.951	0.0%	0.8%	0.661
Malignant Systemic Neoplasm		(n=931)	(n=1,179)		(n=127)	(n=1,983)	
of Kidney or Bladder	Yes	0.2%	1.3%	0.014	0.8%	0.8%	0.999
Malignant Systemic Neoplasm		(n=931)	(n=1,179)		(n=127)	(n=1,983)	
of Prostate	Yes	0.2%	5.3%	<0.001	4.7%	3.0%	0.400
Malignant Systemic Neoplasm		(n=931)	(n=1,179)		(n=127)	(n=1,983)	
of Testicles	Yes	0.0%	0.3%	0.338	0.0%	0.2%	0.999
Malignant Systemic Neoplasm		(n=931)	(n=1,179)		(n=127)	(n=1,983)	
of Connective or Other Soft Tissue	Yes	0.2%	0.1%	0.837	0.0%	0.2%	0.999
Hodgkin's Disease		(n=931)	(n=1,179)		(n=127)	(n=1,983)	
	Yes	0.2%	0.2%	0.999	0.0%	0.2%	0.999
Non-Hodgkin's Lymphoma		(n=931)	(n=1,179)		(n=127)	(n=1,983)	
	Yes	0.1%	0.3%	0.789	0.0%	0.2%	0.999
Other Malignant Systemic		(n=931)	(n=1,179)		(n=127)	(n=1,983)	
Neoplasms of Lymphoid or Histiocytic Tissue	Yes	0.1%	0.4%	0.345	0.0%	0.3%	0.999
All Malignant Skin and		(n=925)	(n=1,164)		(n=126)	(n=1,963)	
Systemic Neoplasms	Yes	11.9%	26.6%	<0.001	6.4%	21.0%	<0.001
All Skin and Systemic		(n=922)	(n=1,156)		(n=126)	(n=1,952)	
Neoplasms	Yes	43.9%	59.5%	<0.001	37.3%	53.6%	<0.001
Prostate-Specific Antigen		(n=927)	(n=1,092)		(n=121)	(n=1,898)	
(continuous)[a]		r=0.258		<0.001	$\bar{x} = 1.16$	$\bar{x} = 1.11$	0.535
(discrete)	Abnormal	2.3%	9.7%	<0.001	6.6%	6.3%	0.999

		Occupation			
Dependent Variable	**Level**	**Officer**	**Enlisted Flyer**	**Enlisted Groundcrew**	**p-Value**
Any Skin Neoplasm		(n=809)	(n=313)	(n=851)	
	Yes	41.2%	33.9%	33.8%	0.004
Malignant Skin Neoplasm		(n=809)	(n=313)	(n=851)	
	Yes	21.3%	16.3%	12.7%	<0.001
Benign Skin Neoplasm		(n=823)	(n=335)	(n=942)	
	Yes	24.7%	19.7%	23.4%	0.193
Skin Neoplasm of Uncertain Behavior or		(n=809)	(n=313)	(n=851)	
Unspecified Nature	Yes	0.4%	0.3%	1.3%	0.060
Any Basal Cell Carcinoma		(n=809)	(n=313)	(n=851)	
	Yes	18.2%	14.4%	9.9%	<0.001
Basal Cell Carcinoma on Ear, Face, Head, or Neck		(n=809)	(n=313)	(n=851)	
	Yes	13.5%	12.5%	7.6%	<0.001
Basal Cell Carcinoma on Trunk		(n=809)	(n=313)	(n=851)	
	Yes	7.2%	2.9%	2.4%	<0.001
Basal Cell Carcinoma on Upper Extremities		(n=809)	(n=313)	(n=851)	
	Yes	5.1%	1.0%	1.8%	<0.001

Table F-2. Dependent Variable-Covariate Associations for the Neoplasia Assessment (Continued)

Dependent Variable	Level	Occupation: Officer	Occupation: Enlisted Flyer	Occupation: Enlisted Groundcrew	p-Value
Basal Cell Carcinoma on Lower Extremities		(n=809)	(n=313)	(n=851)	
	Yes	0.9%	0.0%	0.4%	0.132
Squamous Cell Carcinoma		(n=809)	(n=313)	(n=851)	
	Yes	3.3%	1.6%	1.2%	0.007
Nonmelanoma		(n=809)	(n=313)	(n=851)	
	Yes	20.0%	16.0%	11.5%	<0.001
Melanoma		(n=809)	(n=313)	(n=851)	
	Yes	2.0%	0.3%	1.4%	0.115
Any Systemic Neoplasm		(n=821)	(n=334)	(n=942)	
	Yes	33.9%	31.1%	27.1%	0.008
Malignant Systemic Neoplasm		(n=829)	(n=336)	(n=945)	
	Yes	8.6%	8.6%	4.4%	<0.001
Benign Systemic Neoplasm		(n=821)	(n=334)	(n=942)	
	Yes	25.8%	26.1%	23.0%	0.320
Systemic Neoplasm of Uncertain Behavior or		(n=829)	(n=336)	(n=945)	
Unspecified Nature	Yes	2.9%	0.9%	1.5%	0.031
Malignant Systemic Neoplasm on Eye, Ear, Face,		(n=829)	(n=336)	(n=945)	
Head, or Neck	Yes	1.2%	1.2%	0.7%	0.570
Malignant Systemic Neoplasm of Oral Cavity,		(n=829)	(n=336)	(n=945)	
Pharynx, or Larynx	Yes	0.5%	0.9%	0.4%	0.579
Malignant Systemic Neoplasm of Thymus, Heart, or		(n=829)	(n=336)	(n=945)	
Mediastinum	Yes	0.1%	0.0%	0.1%	0.823
Malignant Systemic Neoplasm of Thyroid Gland		(n=829)	(n=336)	(n=945)	
	Yes	0.4%	0.0%	0.1%	0.318
Malignant Systemic Neoplasm of Bronchus or Lung		(n=829)	(n=336)	(n=945)	
	Yes	0.8%	1.2%	0.2%	0.080
Malignant Systemic Neoplasm of Liver		(n=829)	(n=336)	(n=945)	
	Yes	0.1%	0.3%	0.2%	0.803
Malignant Systemic Neoplasm of Colon or Rectum		(n=829)	(n=336)	(n=945)	
	Yes	0.6%	1.2%	0.6%	0.520
Malignant Systemic Neoplasm of Kidney or Bladder		(n=829)	(n=336)	(n=945)	
	Yes	1.2%	0.9%	0.4%	0.180
Malignant Systemic Neoplasm of Prostate		(n=829)	(n=336)	(n=945)	
	Yes	4.6%	3.3%	1.7%	0.002
Malignant Systemic Neoplasm of Testicles		(n=829)	(n=336)	(n=945)	
	Yes	0.1%	0.3%	0.1%	0.709
Malignant Systemic Neoplasm of Connective or		(n=829)	(n=336)	(n=945)	
Other Soft Tissue	Yes	0.0%	0.3%	0.2%	0.355
Hodgkin's Disease		(n=829)	(n=336)	(n=945)	
	Yes	0.4%	0.0%	0.1%	0.318
Non-Hodgkin's Lymphoma		(n=829)	(n=336)	(n=945)	
	Yes	0.2%	0.0%	0.2%	0.677
Other Malignant Systemic Neoplasms of Lymphoid		(n=829)	(n=336)	(n=945)	
or Histiocytic Tissue	Yes	0.4%	0.3%	0.2%	0.838
All Malignant Skin and Systemic Neoplasms		(n=817)	(n=333)	(n=939)	
	Yes	25.8%	21.0%	14.8%	<0.001
All Skin and Systemic Neoplasms		(n=811)	(n=331)	(n=936)	
	Yes	57.7%	53.2%	48.0%	<0.001

Table F-2. Dependent Variable-Covariate Associations for the Neoplasia Assessment (Continued)

Dependent Variable	Level	Occupation: Officer	Enlisted Flyer	Enlisted Groundcrew	p-Value
Prostate-Specific Antigen		(n=778)	(n=321)	(n=920)	
(continuous)[a]		$\bar{x}$ = 1.22	$\bar{x}$ = 1.24	$\bar{x}$ = 1.00	<0.001
(discrete)	Abnormal	7.7%	7.8%	4.6%	0.014

Dependent Variable	Level	Skin Color: Non-Peach	Peach	p-Value	Hair Color: Black, Dark Brown	Light Brown, Blonde, Red, Bald	p-Value
Any Skin Neoplasm		(n=456)	(n=1,517)		(n=1,345)	(n=626)	
	Yes	28.7%	39.3%	<0.001	35.5%	39.6%	0.090
Malignant Skin Neoplasm		(n=456)	(n=1,517)		(n=1,345)	(n=626)	
	Yes	12.1%	18.2%	0.003	15.5%	19.7%	0.025
Benign Skin Neoplasm		(n=575)	(n=1,525)		(n=1,466)	(n=632)	
	Yes	19.8%	24.6%	0.025	23.3 %	23.1%	0.955
Skin Neoplasm of Uncertain		(n=456)	(n=1,517)		(n=1,345)	(n=626)	
Behavior or Unspecified Nature	Yes	0.7%	0.8%	0.999	0.7%	0.8%	0.999
Any Basal Cell Carcinoma		(n=456)	(n=1,517)		(n=1,345)	(n=626)	
	Yes	10.5%	15.0%	0.019	12.7%	16.8%	0.019
Basal Cell Carcinoma on Ear,		(n=456)	(n=1,517)		(n=1,345)	(n=626)	
Face, Head, or Neck	Yes	7.7%	11.7%	0.018	9.4%	13.7%	0.005
Basal Cell Carcinoma on Trunk		(n=456)	(n=1,517)		(n=1,345)	(n=626)	
	Yes	3.3%	4.8%	0.231	4.0%	5.3%	0.251
Basal Cell Carcinoma on Upper		(n=456)	(n=1,517)		(n=1,345)	(n=626)	
Extremities	Yes	2.4%	3.2%	0.503	2.7%	3.7%	0.286
Basal Cell Carcinoma on Lower		(n=456)	(n=1,517)		(n=1,345)	(n=626)	
Extremities	Yes	0.9%	0.4%	0.371	0.5%	0.6%	0.825
Squamous Cell Carcinoma		(n=456)	(n=1,517)		(n=1,345)	(n=626)	
	Yes	0.9%	2.5%	0.054	1.9%	2.6%	0.469
Nonmelanoma		(n=456)	(n=1,517)		(n=1,345)	(n=626)	
	Yes	11.2%	17.1%	0.003	14.4%	18.7%	0.016
Melanoma		(n=456)	(n=1,517)		(n=1,345)	(n=626)	
	Yes	1.1%	1.6%	0.594	1.4%	1.6%	0.907
Any Systemic Neoplasm		--	--	--	--	--	--
Malignant Systemic Neoplasm		--	--	--	--	--	--
Benign Systemic Neoplasm		--	--	--	--	--	--
Systemic Neoplasm of Uncertain Behavior or Unspecified Nature		--	--	--	--	--	--
Malignant Systemic Neoplasm on Eye, Ear, Face, Head, or Neck		--	--	--	--	--	--

Table F-2. Dependent Variable-Covariate Associations for the Neoplasia Assessment (Continued)

Dependent Variable	Level	Skin Color: Non-Peach	Skin Color: Peach	Skin Color: p-Value	Hair Color: Black, Dark Brown	Hair Color: Light Brown, Blonde, Red, Bald	Hair Color: p-Value
Malignant Systemic Neoplasm of Oral Cavity, Pharynx, or Larynx		--	--	--	--	--	--
Malignant Systemic Neoplasm of Thymus, Heart, and Mediastinum		--	--	--	--	--	--
Malignant Systemic Neoplasm of Thyroid Gland		--	--	--	--	--	--
Malignant Systemic Neoplasm of Bronchus or Lung		--	--	--	--	--	--
Malignant Systemic Neoplasm of Liver		--	--	--	--	--	--
Malignant Systemic Neoplasm of Colon or Rectum		--	--	--	--	--	--
Malignant Systemic Neoplasm of Kidney or Bladder		--	--	--	--	--	--
Malignant Systemic Neoplasm of Prostate		--	--	--	--	--	--
Malignant Systemic Neoplasm of Testicles		--	--	--	--	--	--
Malignant Systemic Neoplasm of Connective or Other Soft Tissue		--	--	--	--	--	--
Hodgkin's Disease		--	--	--	--	--	--
Non-Hodgkin's Lymphoma		--	--	--	--	--	--
Other Malignant Systemic Neoplasms of Lymphoid or Histiocytic Tissue		--	--	--	--	--	--
All Malignant Skin and Systemic Neoplasms	Yes	(n=572) 13.6%	(n=1,517) 22.5%	<0.001	(n=1,460) 18.2%	(n=627) 24.7%	<0.001
All Skin and Systemic Neoplasms	Yes	(n=569) 44.1%	(n=1,509) 55.8%	<0.001	(n=1,453) 51.3%	(n=623) 55.5%	0.088
Prostate-Specific Antigen		--	--	--	--	--	--

Table F-2. Dependent Variable-Covariate Associations for the Neoplasia Assessment (Continued)

Dependent Variable	Level	Eye Color: Brown	Hazel, Green	Gray, Blue	p-Value
Any Skin Neoplasm		(n=604)	(n=523)	(n=846)	
	Yes	32.5%	39.2%	38.5%	0.026
Malignant Skin Neoplasm		(n=604)	(n=523)	(n=846)	
	Yes	13.4%	17.4%	18.8%	0.023
Benign Skin Neoplasm		(n=727)	(n=527)	(n=846)	
	Yes	21.2%	25.2%	23.9%	0.213
Skin Neoplasm of Uncertain		(n=604)	(n=523)	(n=846)	
Behavior or Unspecified Nature	Yes	1.0%	1.3%	0.2%	0.054
Any Basal Cell Carcinoma		(n=604)	(n=523)	(n=846)	
	Yes	10.9%	15.3%	15.4%	0.034
Basal Cell Carcinoma on Ear,		(n=604)	(n=523)	(n=846)	
Face, Head, or Neck	Yes	8.6%	11.1%	12.2%	0.095
Basal Cell Carcinoma on Trunk		(n=604)	(n=523)	(n=846)	
	Yes	3.2%	5.9%	4.4%	0.076
Basal Cell Carcinoma on Upper		(n=604)	(n=523)	(n=846)	
Extremities	Yes	1.2%	4.2%	3.6%	0.005
Basal Cell Carcinoma on Lower		(n=604)	(n=523)	(n=846)	
Extremities	Yes	0.3%	0.6%	0.6%	0.765
Squamous Cell Carcinoma		(n=604)	(n=523)	(n=846)	
	Yes	1.5%	1.9%	2.7%	0.257
Nonmelanoma		(n=604)	(n=523)	(n=846)	
	Yes	12.6%	16.8%	17.3%	0.039
Melanoma		(n=604)	(n=523)	(n=846)	
	Yes	1.0%	1.0%	2.1%	0.109
Any Systemic Neoplasm		--	--	--	--
Malignant Systemic Neoplasm		--	--	--	--
Benign Systemic Neoplasm		--	--	--	--
Systemic Neoplasm of Uncertain Behavior or Unspecified Nature		--	--	--	--
Malignant Systemic Neoplasm on Eye, Ear, Face, Head, or Neck		--	--	--	--
Malignant Systemic Neoplasm of Oral Cavity, Pharynx, or Larynx		--	--	--	--
Malignant Systemic Neoplasm of Thymus, Heart, and Mediastinum		--	--	--	--
Malignant Systemic Neoplasm of Thyroid Gland		--	--	--	--
Malignant Systemic Neoplasm of Bronchus or Lung		--	--	--	--
Malignant Systemic Neoplasm of Liver		--	--	--	--
Malignant Systemic Neoplasm of Colon or Rectum		--	--	--	--
Malignant Systemic Neoplasm of Kidney or Bladder		--	--	--	--

Table F-2. Dependent Variable-Covariate Associations for the Neoplasia Assessment (Continued)

Dependent Variable	Level	Eye Color: Brown	Hazel, Green	Gray, Blue	p-Value
Malignant Systemic Neoplasm of Prostate		--	--	--	--
Malignant Systemic Neoplasm of Testicles		--	--	--	--
Malignant Systemic Neoplasm of Connective or Other Soft Tissue		--	--	--	--
Hodgkin's Disease		--	--	--	--
Non-Hodgkin's Lymphoma		--	--	--	--
Other Malignant Systemic Neoplasms of Lymphoid or Histiocytic Tissue		--	--	--	--
All Malignant Skin and Systemic Neoplasms	Yes	(n=724) 14.4%	(n=525) 23.2%	(n=840) 23.1%	<0.001
All Skin and Systemic Neoplasms	Yes	(n=722) 45.4%	(n=520) 57.7%	(n=836) 55.6%	<0.001
Prostate-Specific Antigen		--	--	--	--

Dependent Variable	Level	Skin Reaction to Sun after First Exposure: No Reaction	Some Redness Only	Burns	Painfully Burns	p-Value
Any Skin Neoplasm	Yes	(n=715) 30.8%	(n=796) 37.6%	(n=301) 43.5%	(n=160) 48.1%	<0.001
Malignant Skin Neoplasm	Yes	(n=715) 9.8%	(n=796) 18.5%	(n=301) 23.6%	(n=160) 26.9%	<0.001
Benign Skin Neoplasm	Yes	(n=819) 22.2%	(n=809) 22.7%	(n=311) 25.1%	(n=160) 28.1%	0.346
Skin Neoplasm of Uncertain Behavior or Unspecified Nature	Yes	(n=715) 0.7%	(n=796) 0.9%	(n=301) 0.7%	(n=160) 0.6%	0.967
Any Basal Cell Carcinoma	Yes	(n=715) 8.1%	(n=796) 15.0%	(n=301) 20.9%	(n=160) 22.5%	<0.001
Basal Cell Carcinoma on Ear, Face, Head, or Neck	Yes	(n=715) 6.2%	(n=796) 11.3%	(n=301) 16.3%	(n=160) 18.8%	<0.001
Basal Cell Carcinoma on Trunk	Yes	(n=715) 2.5%	(n=796) 4.8%	(n=301) 6.3%	(n=160) 7.5%	0.006
Basal Cell Carcinoma on Upper Extremities	Yes	(n=715) 1.3%	(n=796) 3.4%	(n=301) 4.3%	(n=160) 6.3%	<0.001
Basal Cell Carcinoma on Lower Extremities	Yes	(n=715) 0.0%	(n=796) 1.0%	(n=301) 0.3%	(n=160) 0.6%	0.051
Squamous Cell Carcinoma	Yes	(n=715) 1.3%	(n=796) 1.9%	(n=301) 3.3%	(n=160) 5.0%	0.011
Nonmelanoma	Yes	(n=715) 9.1%	(n=796) 17.0%	(n=301) 22.9%	(n=160) 25.6%	<0.001
Melanoma	Yes	(n=715) 0.8%	(n=796) 2.0%	(n=301) 1.0%	(n=160) 2.5%	0.158
Any Systemic Neoplasm		--	--	--	--	--

Table F-2. Dependent Variable-Covariate Associations for the Neoplasia Assessment (Continued)

Dependent Variable	Level	Skin Reaction to Sun after First Exposure: No Reaction	Some Redness Only	Burns	Painfully Burns	p-Value
Malignant Systemic Neoplasm		--	--	--	--	--
Benign Systemic Neoplasm		--	--	--	--	--
Systemic Neoplasm of Uncertain Behavior or Unspecified Nature		--	--	--	--	--
Malignant Systemic Neoplasm on Eye, Ear, Face, Head, or Neck		--	--	--	--	--
Malignant Systemic Neoplasm of Oral Cavity, Pharynx, or Larynx		--	--	--	--	--
Malignant Systemic Neoplasm of Thymus, Heart, and Mediastinum		--	--	--	--	--
Malignant Systemic Neoplasm of Thyroid Gland		--	--	--	--	--
Malignant Systemic Neoplasm of Bronchus or Lung		--	--	--	--	--
Malignant Systemic Neoplasm of Liver		--	--	--	--	--
Malignant Systemic Neoplasm of Colon or Rectum		--	--	--	--	--
Malignant Systemic Neoplasm of Kidney or Bladder		--	--	--	--	--
Malignant Systemic Neoplasm of Prostate		--	--	--	--	--
Malignant Systemic Neoplasm of Testicles		--	--	--	--	--
Malignant Systemic Neoplasm of Connective or Other Soft Tissue		--	--	--	--	--
Hodgkin's Disease		--	--	--	--	--
Non-Hodgkin's Lymphoma		--	--	--	--	--
Other Malignant Systemic Neoplasms of Lymphoid or Histiocytic Tissue		--	--	--	--	--
All Malignant Skin and Systemic Neoplasms	Yes	(n=813) 13.3%	(n=806) 22.2%	(n=310) 26.8%	(n=159) 31.5%	<0.001
All Skin and Systemic Neoplasms	Yes	(n=806) 47.5%	(n=804) 53.9%	(n=308) 59.1%	(n=159) 59.8%	<0.001
Prostate-Specific Antigen		--	--	--	--	--

Table F-2. Dependent Variable-Covariate Associations for the Neoplasia Assessment (Continued)

Dependent Variable	Level	Skin Reaction to Sun after Repeated Exposure				
		Deep Tan	Moderate Tan	Mild Tan	Freckles	p-Value
Any Skin Neoplasm		(n=553)	(n=980)	(n=368)	(n=71)	
	Yes	31.1%	36.7%	43.2%	50.7%	<0.001
Malignant Skin Neoplasm		(n=553)	(n=980)	(n=368)	(n=71)	
	Yes	9.2%	16.1%	26.4%	35.2%	<0.001
Benign Skin Neoplasm		(n=620)	(n=1,011)	(n=383)	(n=85)	
	Yes	23.4%	24.0%	21.2%	23.5%	0.728
Skin Neoplasm of Uncertain Behavior or		(n=553)	(n=980)	(n=368)	(n=71)	
Unspecified Nature	Yes	1.1%	0.5%	0.5%	2.8%	0.122
Any Basal Cell Carcinoma		(n=553)	(n=980)	(n=368)	(n=71)	
	Yes	7.6%	13.2%	22.8%	29.6%	<0.001
Basal Cell Carcinoma on Ear, Face, Head, or		(n=553)	(n=980)	(n=368)	(n=71)	
Neck	Yes	6.5%	10.2%	15.8%	26.8%	<0.001
Basal Cell Carcinoma on Trunk		(n=553)	(n=980)	(n=368)	(n=71)	
	Yes	1.6%	4.5%	7.1%	11.3%	<0.001
Basal Cell Carcinoma on Upper Extremities		(n=553)	(n=980)	(n=368)	(n=71)	
	Yes	0.9%	3.2%	5.2%	5.6%	<0.001
Basal Cell Carcinoma on Lower Extremities		(n=553)	(n=980)	(n=368)	(n=71)	
	Yes	0.5%	0.3%	0.8%	1.4%	0.452
Squamous Cell Carcinoma		(n=553)	(n=980)	(n=368)	(n=71)	
	Yes	0.9%	2.1%	2.7%	8.5%	<0.001
Nonmelanoma		(n=553)	(n=980)	(n=368)	(n=71)	
	Yes	8.7%	14.8%	25.3%	33.8%	<0.001
Melanoma		(n=553)	(n=980)	(n=368)	(n=71)	
	Yes	0.9%	1.7%	1.4%	2.8%	0.455
Any Systemic Neoplasm		--	--	--	--	--
Malignant Systemic Neoplasm		--	--	--	--	--
Benign Systemic Neoplasm		--	--	--	--	--
Systemic Neoplasm of Uncertain Behavior or Unspecified Nature		--	--	--	--	--
Malignant Systemic Neoplasm on Eye, Ear, Face, Head, or Neck		--	--	--	--	--
Malignant Systemic Neoplasm of Oral Cavity, Pharynx, or Larynx		--	--	--	--	--
Malignant Systemic Neoplasm of Thymus, Heart, or Mediastinum		--	--	--	--	--
Malignant Systemic Neoplasm of Thyroid Gland		--	--	--	--	--
Malignant Systemic Neoplasm of Bronchus or Lung		--	--	--	--	--
Malignant Systemic Neoplasm of Liver		--	--	--	--	--
Malignant Systemic Neoplasm of Colon or Rectum		--	--	--	--	--
Malignant Systemic Neoplasm of Kidney or Bladder		--	--	--	--	--

Table F-2. Dependent Variable-Covariate Associations for the Neoplasia Assessment (Continued)

Dependent Variable	Level	Skin Reaction to Sun after Repeated Exposure: Deep Tan	Moderate Tan	Mild Tan	Freckles	p-Value
Malignant Systemic Neoplasm of Prostate		--	--	--	--	--
Malignant Systemic Neoplasm of Testicles		--	--	--	--	--
Malignant Systemic Neoplasm of Connective or Other Soft Tissue		--	--	--	--	--
Hodgkin's Disease		--	--	--	--	--
Non-Hodgkin's Lymphoma		--	--	--	--	--
Other Malignant Systemic Neoplasms of Lymphoid or Histiocytic Tissue		--	--	--	--	--
All Malignant Skin and Systemic Neoplasms		(n=617)	(n=1,005)	(n=382)	(n=84)	
	Yes	13.9%	19.7%	28.8%	31.0%	<0.001
All Skin and Systemic Neoplasms		(n=613)	(n=999)	(n=381)	(n=84)	
	Yes	48.6%	52.5%	58.5%	57.1%	0.019
Prostate-Specific Antigen		--	--	--	--	--

Dependent Variable	Level	Composite Skin-Reaction Index: Low	Medium	High	p-Value
Any Skin Neoplasm		(n=1,304)	(n=471)	(n=197)	
	Yes	33.4%	41.4%	48.7%	<0.001
Malignant Skin Neoplasm		(n=1,304)	(n=471)	(n=197)	
	Yes	13.0%	22.5%	27.9%	<0.001
Benign Skin Neoplasm		(n=1,394)	(n=494)	(n=211)	
	Yes	22.9%	22.7%	27.5%	0.314
Skin Neoplasm of Uncertain Behavior or Unspecified Nature		(n=1,304)	(n=471)	(n=197)	
	Yes	0.8%	0.6%	1.0%	0.876
Any Basal Cell Carcinoma		(n=1,304)	(n=471)	(n=197)	
	Yes	10.5%	19.8%	23.4%	<0.001
Basal Cell Carcinoma on Ear, Face, Head, or Neck		(n=1,304)	(n=471)	(n=197)	
	Yes	8.5%	13.6%	19.3%	<0.001
Basal Cell Carcinoma on Trunk		(n=1,304)	(n=471)	(n=197)	
	Yes	3.2%	5.7%	9.1%	<0.001
Basal Cell Carcinoma on Upper Extremities		(n=1,304)	(n=471)	(n=197)	
	Yes	2.0%	4.5%	6.1%	<0.001
Basal Cell Carcinoma on Lower Extremities		(n=1,304)	(n=471)	(n=197)	
	Yes	0.4%	0.6%	1.0%	0.458
Squamous Cell Carcinoma		(n=1,304)	(n=471)	(n=197)	
	Yes	1.5%	2.3%	5.6%	<0.001
Nonmelanoma		(n=1,304)	(n=471)	(n=197)	
	Yes	11.9%	21.9%	26.4%	<0.001
Melanoma		(n=1,304)	(n=471)	(n=197)	
	Yes	1.5%	0.9%	3.1%	0.099
Any Systemic Neoplasm		--	--	--	--

Table F-2. Dependent Variable-Covariate Associations for the Neoplasia Assessment (Continued)

		Composite Skin-Reaction Index			
Dependent Variable	**Level**	**Low**	**Medium**	**High**	**p-Value**
Malignant Systemic Neoplasm		--	--	--	--
Benign Systemic Neoplasm		--	--	--	--
Systemic Neoplasm of Uncertain Behavior or Unspecified Nature		--	--	--	--
Malignant Systemic Neoplasm on Eye, Ear, Face, Head, or Neck		--	--	--	--
Malignant Systemic Neoplasm of Oral Cavity, Pharynx, or Larynx		--	--	--	--
Malignant Systemic Neoplasm of Thymus, Heart, or Mediastinum		--	--	--	--
Malignant Systemic Neoplasm of Thyroid Gland		--	--	--	--
Malignant Systemic Neoplasm of Bronchus or Lung		--	--	--	--
Malignant Systemic Neoplasm of Liver		--	--	--	--
Malignant Systemic Neoplasm of Colon or Rectum		--	--	--	--
Malignant Systemic Neoplasm of Kidney or Bladder		--	--	--	--
Malignant Systemic Neoplasm of Prostate		--	--	--	--
Malignant Systemic Neoplasm of Testicles		--	--	--	--
Malignant Systemic Neoplasm of Connective or Other Soft Tissue		--	--	--	--
Hodgkin's Disease		--	--	--	--
Non-Hodgkin's Lymphoma		--	--	--	--
Other Malignant Systemic Neoplasms of Lymphoid or Histiocytic Tissue		--	--	--	--
All Malignant Skin and Systemic Neoplasms		(n=1,386)	(n=493)	(n=209)	
	Yes	16.7%	25.6%	29.7%	<0.001
All Skin and Systemic Neoplasms		(n=1,378)	(n=490)	(n=209)	
	Yes	50.0%	56.9%	59.8%	0.003
Prostate-Specific Antigen		--	--	--	--

Table F-2. Dependent Variable-Covariate Associations for the Neoplasia Assessment (Continued)

Dependent Variable	Level	Average Lifetime Residential History			Ionizing Radiation Exposure		
		<37°	≥37°	p-Value	No	Yes	p-Value
Any Skin Neoplasm		(n=993)	(n=980)		(n=1,484)	(n=489)	
	Yes	39.5%	34.2%	0.017	34.9%	42.7%	0.002
Malignant Skin Neoplasm		(n=993)	(n=980)		(n=1,484)	(n=489)	
	Yes	20.3%	13.2%	<0.001	15.7%	20.0%	0.031
Benign Skin Neoplasm		(n=1,073)	(n=1,027)		(n=1,572)	(n=528)	
	Yes	22.7%	23.9%	0.580	22.5%	25.8%	0.135
Skin Neoplasm of Uncertain		(n=993)	(n=980)		(n=1,484)	(n=489)	
Behavior or Unspecified Nature	Yes	0.6%	0.9%	0.586	0.7%	1.0%	0.639
Any Basal Cell Carcinoma		(n=993)	(n=980)		(n=1,484)	(n=489)	
	Yes	17.9%	10.0%	<0.001	13.1%	16.6%	0.069
Basal Cell Carcinoma on Ear, Face,		(n=993)	(n=980)		(n=1,484)	(n=489)	
Head, or Neck	Yes	14.1%	7.5%	<0.001	10.0%	13.3%	0.049
Basal Cell Carcinoma on Trunk		(n=993)	(n=980)		(n=1,484)	(n=489)	
	Yes	5.9%	2.9%	<0.001	4.3%	4.7%	0.812
Basal Cell Carcinoma on Upper		(n=993)	(n=980)		(n=1,484)	(n=489)	
Extremities	Yes	3.8%	2.1%	0.039	3.2%	2.5%	0.516
Basal Cell Carcinoma on Lower		(n=993)	(n=980)		(n=1,484)	(n=489)	
Extremities	Yes	0.5%	0.5%	0.999	0.6%	0.2%	0.472
Squamous Cell Carcinoma		(n=993)	(n=980)		(n=1,484)	(n=489)	
	Yes	3.0%	1.2%	0.009	2.0%	2.7%	0.450
Nonmelanoma		(n=993)	(n=980)		(n=1,484)	(n=489)	
	Yes	19.9%	11.4%	<0.001	14.9%	18.2%	0.095
Melanoma		(n=993)	(n=980)		(n=1,484)	(n=489)	
	Yes	0.7%	2.2%	0.008	1.3%	2.0%	0.316
Any Systemic Neoplasm					(n=1,565)	(n=532)	
	Yes	--	--	--	29.8%	32.0%	0.389
Malignant Systemic Neoplasm					(n=1,573)	(n=537)	
	Yes	--	--	--	5.8%	9.5%	0.004
Benign Systemic Neoplasm					(n=1,565)	(n=532)	
	Yes	--	--	--	24.6%	24.6%	0.999
Systemic Neoplasm of Uncertain					(n=1,573)	(n=537)	
Behavior or Unspecified Nature	Yes	--	--	--	1.9%	2.1%	0.981
Malignant Systemic Neoplasm on					(n=1,573)	(n=537)	
Eye, Ear, Face, Head, or Neck	Yes	--	--	--	0.9%	1.3%	0.561
Malignant Systemic Neoplasm of					(n=1,573)	(n=537)	
Oral Cavity, Pharynx, or Larynx	Yes	--	--	--	0.3%	1.1%	0.061
Malignant Systemic Neoplasm of					(n=1,573)	(n=537)	
Thymus, Heart, or Mediastinum	Yes	--	--	--	0.1%	0.2%	0.999
Malignant Systemic Neoplasm of					(n=1,573)	(n=537)	
Thyroid Gland	Yes	--	--	--	0.3%	0.0%	0.552
Malignant Systemic Neoplasm of					(n=1,573)	(n=537)	
Bronchus or Lung	Yes	--	--	--	0.5%	0.9%	0.447
Malignant Systemic Neoplasm of					(n=1,573)	(n=537)	
Liver	Yes	--	--	--	0.1%	0.4%	0.580
Malignant Systemic Neoplasm of					(n=1,573)	(n=537)	
Colon or Rectum	Yes	--	--	--	0.6%	1.1%	0.317

Table F-2. Dependent Variable-Covariate Associations for the Neoplasia Assessment (Continued)

Dependent Variable	Level	Average Lifetime Residential History			Ionizing Radiation Exposure		
		<37°	≥37°	p-Value	No	Yes	p-Value
Malignant Systemic Neoplasm of Kidney or Bladder	Yes	--	--	--	(n=1,573) 0.6%	(n=537) 1.5%	0.076
Malignant Systemic Neoplasm of Prostate	Yes	--	--	--	(n=1,573) 2.6%	(n=537) 4.5%	0.044
Malignant Systemic Neoplasm of Testicles	Yes	--	--	--	(n=1,573) 0.2%	(n=537) 0.0%	0.727
Malignant Systemic Neoplasm of Connective or Other Soft Tissue	Yes	--	--	--	(n=1,573) 0.1%	(n=537) 0.4%	0.329
Hodgkin's Disease	Yes	--	--	--	(n=1,573) 0.2%	(n=537) 0.2%	0.999
Non-Hodgkin's Lymphoma	Yes	--	--	--	(n=1,573) 0.2%	(n=537) 0.2%	0.999
Other Malignant Systemic Neoplasms of Lymphoid or Histiocytic Tissue	Yes	--	--	--	(n=1,573) 0.3%	(n=537) 0.4%	0.999
All Malignant Skin and Systemic Neoplasms	Yes	(n=1,067) 23.0%	(n=1,022) 17.1%	<0.001	(n=1,562) 18.6%	(n=527) 24.5%	0.005
All Skin and Systemic Neoplasms	Yes	(n=1,061) 54.3%	(n=1,017) 50.8%	0.126	(n=1,556) 51.0%	(n=522) 57.3%	0.015
Prostate-Specific Antigen					(n=1,518)	(n=501)	
(continuous)[a]					$\bar{x} = 1.10$	$\bar{x} = 1.17$	0.112
(discrete)	Abnormal	--	--	--	6.0%	7.2%	0.398

Dependent Variable	Level	Industrial Chemicals Exposure			Herbicide Exposure		
		No	Yes	p-Value	No	Yes	p-Value
Any Skin Neoplasm	Yes	(n=759) 36.6%	(n=1,214) 37.0%	0.910	--	--	--
Malignant Skin Neoplasm	Yes	(n=759) 17.1%	(n=1,214) 16.6%	0.788	--	--	--
Benign Skin Neoplasm	Yes	(n=796) 23.6%	(n=1,304) 23.1%	0.819	--	--	--
Skin Neoplasm of Uncertain Behavior or Unspecified Nature	Yes	(n=759) 0.4%	(n=1,214) 1.0%	0.226	--	--	--
Any Basal Cell Carcinoma	Yes	(n=759) 14.6%	(n=1,214) 13.6%	0.564	--	--	--
Basal Cell Carcinoma on Ear, Face, Head, or Neck	Yes	(n=759) 10.9%	(n=1,214) 10.7%	0.933	--	--	--
Basal Cell Carcinoma on Trunk	Yes	(n=759) 5.1%	(n=1,214) 4.0%	0.257	--	--	--
Basal Cell Carcinoma on Upper Extremities	Yes	(n=759) 3.4%	(n=1,214) 2.7%	0.446	--	--	--
Basal Cell Carcinoma on Lower Extremities	Yes	(n=759) 0.5%	(n=1,214) 0.5%	0.999	--	--	--

Table F-2. Dependent Variable-Covariate Associations for the Neoplasia Assessment (Continued)

Dependent Variable	Level	Industrial Chemicals Exposure			Herbicide Exposure		
		No	Yes	p-Value	No	Yes	p-Value
Squamous Cell Carcinoma		(n=759)	(n=1,214)				
	Yes	2.6%	1.8%	0.284	--	--	--
Nonmelanoma		(n=759)	(n=1,214)				
	Yes	16.5%	15.2%	0.505	--	--	--
Melanoma		(n=759)	(n=1,214)				
	Yes	1.2%	1.7%	0.524	--	--	--
Any Systemic Neoplasm					(n=762)	(n=1,335)	
	Yes	--	--	--	26.4%	32.7%	0.003
Malignant Systemic Neoplasm					(n=765)	(n=1,345)	
	Yes	--	--	--	4.6%	8.0%	0.004
Benign Systemic Neoplasm					(n=762)	(n=1,335)	
	Yes	--	--	--	22.1%	26.1%	0.045
Systemic Neoplasm of Uncertain					(n=765)	(n=1,345)	
Behavior or Unspecified Nature	Yes	--	--	--	1.4%	2.2%	0.270
Malignant Systemic Neoplasm on					(n=765)	(n=1,345)	
Eye, Ear, Face, Head, or Neck	Yes	--	--	--	0.8%	1.1%	0.611
Malignant Systemic Neoplasm of					(n=765)	(n=1,345)	
Oral Cavity, Pharynx, or Larynx	Yes	--	--	--	0.3%	0.7%	0.349
Malignant Systemic Neoplasm of					(n=765)	(n=1,345)	
Thymus, Heart, or Mediastinum	Yes	--	--	--	0.0%	0.2%	0.740
Malignant Systemic Neoplasm of					(n=765)	(n=1,345)	
Thyroid Gland	Yes	--	--	--	0.3%	0.2%	0.959
Malignant Systemic Neoplasm of					(n=765)	(n=1,345)	
Bronchus or Lung	Yes	--	--	--	0.1%	0.9%	0.063
Malignant Systemic Neoplasm of					(n=765)	(n=1,345)	
Liver	Yes	--	--	--	0.0%	0.3%	0.323
Malignant Systemic Neoplasm of					(n=765)	(n=1,345)	
Colon or Rectum	Yes	--	--	--	0.7%	0.7%	0.999
Malignant Systemic Neoplasm of					(n=765)	(n=1,345)	
Kidney or Bladder	Yes	--	--	--	0.4%	1.0%	0.177
Malignant Systemic Neoplasm of					(n=765)	(n=1,345)	
Prostate	Yes	--	--	--	2.0%	3.7%	0.035
Malignant Systemic Neoplasm of					(n=765)	(n=1,345)	
Testicles	Yes	--	--	--	0.0%	0.2%	0.480
Malignant Systemic Neoplasm of					(n=765)	(n=1,345)	
Connective or Other Soft Tissue	Yes	--	--	--	0.1%	0.2%	0.999
Hodgkin's Disease					(n=765)	(n=1,345)	
	Yes	--	--	--	0.1%	0.2%	0.999
Non-Hodgkin's Lymphoma					(n=765)	(n=1,345)	
	Yes	--	--	--	0.1%	0.2%	0.999
Other Malignant Systemic					(n=765)	(n=1,345)	
Neoplasms of Lymphoid or Histiocytic Tissue	Yes	--	--	--	0.3%	0.3%	0.999
All Malignant Skin and Systemic		(n=794)	(n=1,295)		(n=762)	(n=1,327)	
Neoplasms	Yes	21.0%	19.5%	0.440	15.8%	22.6%	<0.001
All Skin and Systemic Neoplasms		(n=789)	(n=1,289)		(n=759)	(n=1,319)	
	Yes	54.3%	51.6%	0.258	45.9%	56.5%	<0.001

Table F-2. Dependent Variable-Covariate Associations for the Neoplasia Assessment (Continued)

Dependent Variable	Level	Industrial Chemicals Exposure No	Industrial Chemicals Exposure Yes	Industrial Chemicals Exposure p-Value	Herbicide Exposure No	Herbicide Exposure Yes	Herbicide Exposure p-Value
Prostate-Specific Antigen					(n=739)	(n=1,280)	
(continuous)[a]		--	--	--	$\bar{x}$ = 1.12	$\bar{x}$ = 1.11	0.808
(discrete)	Abnormal	--	--	--	5.8%	6.6%	0.570

Dependent Variable	Level	Lifetime Cigarette Smoking History (pack-years) 0	>0–10	>10	p-Value
Any Skin Neoplasm		--	--	--	--
Malignant Skin Neoplasm		--	--	--	--
Benign Skin Neoplasm		--	--	--	--
Skin Neoplasm of Uncertain Behavior or Unspecified Nature		--	--	--	--
Any Basal Cell Carcinoma		--	--	--	--
Basal Cell Carcinoma on Ear, Face, Head, or Neck		--	--	--	--
Basal Cell Carcinoma on Trunk		--	--	--	--
Basal Cell Carcinoma on Upper Extremities		--	--	--	--
Basal Cell Carcinoma on Lower Extremities		--	--	--	--
Squamous Cell Carcinoma		--	--	--	--
Nonmelanoma		--	--	--	--
Melanoma		--	--	--	--
Any Systemic Neoplasm		(n=589)	(n=553)	(n=952)	
	Yes	29.4%	28.8%	31.9%	0.357
Malignant Systemic Neoplasm		(n=592)	(n=556)	(n=959)	
	Yes	5.4%	4.1%	9.1%	<0.001
Benign Systemic Neoplasm		(n=589)	(n=553)	(n=952)	
	Yes	25.0%	25.1%	24.1%	0.870
Systemic Neoplasm of Uncertain Behavior or Unspecified Nature		(n=592)	(n=556)	(n=959)	
	Yes	1.4%	1.6%	2.5%	0.227
Malignant Systemic Neoplasm on Eye, Ear, Face, Head, or Neck		(n=592)	(n=556)	(n=959)	
	Yes	1.0%	0.4%	1.4%	0.170
Malignant Systemic Neoplasm of Oral Cavity, Pharynx, or Larynx		(n=592)	(n=556)	(n=959)	
	Yes	0.3%	0.2%	0.8%	0.179
Malignant Systemic Neoplasm of Thymus, Heart, and Mediastinum		(n=592)	(n=556)	(n=959)	
	Yes	0.0%	0.0%	0.2%	0.302
Malignant Systemic Neoplasm of Thyroid Gland		(n=592)	(n=556)	(n=959)	
	Yes	0.5%	0.0%	0.1%	0.102

Table F-2. Dependent Variable-Covariate Associations for the Neoplasia Assessment (Continued)

Dependent Variable	Level	Lifetime Cigarette Smoking History (pack-years) 0	>0–10	>10	p-Value
Malignant Systemic Neoplasm of Bronchus or Lung		(n=592)	(n=556)	(n=959)	
	Yes	0.0%	0.0%	1.4%	<0.001
Malignant Systemic Neoplasm of Liver		(n=592)	(n=556)	(n=959)	
	Yes	0.0%	0.2%	0.3%	0.388
Malignant Systemic Neoplasm of Colon or Rectum		(n=592)	(n=556)	(n=959)	
	Yes	0.7%	0.5%	0.8%	0.800
Malignant Systemic Neoplasm of Kidney or Bladder		(n=592)	(n=556)	(n=959)	
	Yes	0.0%	0.4%	1.6%	<0.001
Malignant Systemic Neoplasm of Prostate		(n=592)	(n=556)	(n=959)	
	Yes	3.0%	1.4%	4.1%	0.017
Malignant Systemic Neoplasm of Testicles		(n=592)	(n=556)	(n=959)	
	Yes	0.0%	0.2%	0.2%	0.550
Malignant Systemic Neoplasm of Connective or		(n=592)	(n=556)	(n=959)	
Other Soft Tissue	Yes	0.0%	0.2%	0.2%	0.550
Hodgkin's Disease		(n=592)	(n=556)	(n=959)	
	Yes	0.3%	0.2%	0.1%	0.589
Non-Hodgkin's Lymphoma		(n=592)	(n=556)	(n=959)	
	Yes	0.3%	0.4%	0.0%	0.187
Other Malignant Systemic Neoplasms of Lymphoid		(n=592)	(n=556)	(n=959)	
or Histiocytic Tissue	Yes	0.2%	0.4%	0.3%	0.812
All Malignant Skin and Systemic Neoplasms		(n=585)	(n=552)	(n=949)	
	Yes	20.7%	17.4%	21.4%	0.163
All Skin and Systemic Neoplasms		(n=583)	(n=549)	(n=943)	
	Yes	52.0%	51.7%	53.6%	0.740
Prostate-Specific Antigen		(n=569)	(n=542)	(n=906)	
(continuous)[a]			r=-0.016		0.468
(discrete)	Abnormal	7.7%	5.2%	6.0%	0.187

Dependent Variable	Level	Lifetime Alcohol History (drink-years) 0	>0–40	>40	p-Value
Any Skin Neoplasm					
		--	--	--	--
Malignant Skin Neoplasm					
		--	--	--	--
Benign Skin Neoplasm					
		--	--	--	--
Skin Neoplasm of Uncertain Behavior or					
Unspecified Nature		--	--	--	--
Any Basal Cell Carcinoma					
		--	--	--	--
Basal Cell Carcinoma on Ear, Face, Head, or					
Neck		--	--	--	--
Basal Cell Carcinoma on Trunk					
		--	--	--	--
Basal Cell Carcinoma on Upper Extremities					
		--	--	--	--

Table F-2. Dependent Variable-Covariate Associations for the Neoplasia Assessment (Continued)

Dependent Variable	Level	Lifetime Alcohol History (drink-years) 0	>0–40	>40	p-Value
Basal Cell Carcinoma on Lower Extremities		--	--	--	--
Squamous Cell Carcinoma		--	--	--	--
Nonmelanoma		--	--	--	--
Melanoma		--	--	--	--
Any Systemic Neoplasm		(n=115)	(n=1,368)	(n=607)	
	Yes	34.8%	30.4%	29.5%	0.527
Malignant Systemic Neoplasm		(n=118)	(n=1,374)	(n=610)	
	Yes	6.8%	6.3%	7.7%	0.494
Benign Systemic Neoplasm		(n=115)	(n=1,368)	(n=607)	
	Yes	30.4%	24.6%	23.6%	0.292
Systemic Neoplasm of Uncertain Behavior or		(n=118)	(n=1,374)	(n=610)	
Unspecified Nature	Yes	0.0%	1.9%	2.5%	0.202
Malignant Systemic Neoplasm on Eye, Ear,		(n=118)	(n=1,374)	(n=610)	
Face, Head, or Neck	Yes	0.0%	1.0%	1.3%	0.400
Malignant Systemic Neoplasm of Oral Cavity,		(n=118)	(n=1,374)	(n=610)	
Pharynx, or Larynx	Yes	0.0%	0.4%	0.8%	0.397
Malignant Systemic Neoplasm of Thymus,		(n=118)	(n=1,374)	(n=610)	
Heart, or Mediastinum	Yes	0.0%	0.2%	0.0%	0.588
Malignant Systemic Neoplasm of Thyroid		(n=118)	(n=1,374)	(n=610)	
Gland	Yes	0.0%	0.2%	0.2%	0.859
Malignant Systemic Neoplasm of Bronchus or		(n=118)	(n=1,374)	(n=610)	
Lung	Yes	0.0%	0.7%	0.5%	0.560
Malignant Systemic Neoplasm of Liver		(n=118)	(n=1,374)	(n=610)	
	Yes	0.0%	0.2%	0.2%	0.859
Malignant Systemic Neoplasm of Colon or		(n=118)	(n=1,374)	(n=610)	
Rectum	Yes	0.9%	0.7%	0.8%	0.908
Malignant Systemic Neoplasm of Kidney or		(n=118)	(n=1,374)	(n=610)	
Bladder	Yes	3.4%	0.2%	1.6%	<0.001
Malignant Systemic Neoplasm of Prostate		(n=118)	(n=1,374)	(n=610)	
	Yes	1.7%	3.0%	3.4%	0.585
Malignant Systemic Neoplasm of Testicles		(n=118)	(n=1,374)	(n=610)	
	Yes	0.0%	0.2%	0.0%	0.451
Malignant Systemic Neoplasm of Connective		(n=118)	(n=1,374)	(n=610)	
or Other Soft Tissue	Yes	0.9%	0.2%	0.0%	0.083
Hodgkin's Disease		(n=118)	(n=1,374)	(n=610)	
	Yes	0.0%	0.2%	0.2%	0.859
Non-Hodgkin's Lymphoma		(n=118)	(n=1,374)	(n=610)	
	Yes	0.0%	0.2%	0.3%	0.613
Other Malignant Systemic Neoplasms of		(n=118)	(n=1,374)	(n=610)	
Lymphoid or Histiocytic Tissue	Yes	0.0%	0.3%	0.3%	0.828
All Malignant Skin and Systemic Neoplasms		(n=115)	(n=1,364)	(n=602)	
	Yes	19.1%	19.7%	21.3%	0.688
All Skin and Systemic Neoplasms		(n=113)	(n=1,358)	(n=600)	
	Yes	54.0%	52.7%	52.3%	0.949

Table F-2. Dependent Variable-Covariate Associations for the Neoplasia Assessment (Continued)

		Lifetime Alcohol History (drink-years)			
Dependent Variable	**Level**	**0**	**>0–40**	**>40**	**p-Value**
Prostate-Specific Antigen		(n=112)	(n=1,317)	(n=583)	
(continuous)[a]			r=-0.011		0.616
(discrete)	Abnormal	7.1%	6.5%	5.8%	0.818

[a] Analysis performed on natural logarithm scale; means transformed from natural logarithm scale.

--: Covariate not applicable for dependent variable.

Note: Correlations (r) are based on total sample size and are not category-specific.

Table F-3. Dependent Variable-Covariate Associations for the Neurology Assessment

Dependent Variable	Level	Age: Born ≥1942	Age: Born <1942	Age: p-Value	Race: Black	Race: Non-Black	Race: p-Value
Inflammatory Diseases		(n=926)	(n=1,182)		(n=128)	(n=1,980)	
	Yes	0.4%	0.3%	0.999	0.0%	0.4%	0.999
Hereditary and		(n=929)	(n=1,186)		(n=128)	(n=1,987)	
Degenerative Diseases	Yes	7.0 %	10.4%	0.009	7.0%	9.0%	0.547
Peripheral Disorders		(n=928)	(n=1,182)		(n=128)	(n=1,982)	
	Yes	14.9%	24.6%	<0.001	17.2%	20.5%	0.424
Other Neurological		(n=925)	(n=1,181)		(n=127)	(n=1,979)	
Disorders	Yes	13.4%	22.0%	<0.001	33.1%	17.3%	<0.001
Smell		(n=926)	(n=1,183)		(n=128)	(n=1,981)	
	Abnormal	1.6%	2.0%	0.597	3.1%	1.8%	0.443
Visual Fields		(n=928)	(n=1,183)		(n=127)	(n=1,984)	
	Abnormal	0.2%	0.4%	0.660	1.6%	0.3%	0.086
Light Reaction		(n=926)	(n=1,182)		(n=128)	(n=1,980)	
	Abnormal	0.4%	0.8%	0.497	2.3%	0.5%	0.046
Ocular Movement		(n=929)	(n=1,186)		(n=128)	(n=1,987)	
	Abnormal	1.2%	1.7%	0.440	0.8%	1.5%	0.775
Facial Sensation		(n=929)	(n=1,184)		(n=128)	(n=1,985)	
	Abnormal	0.0%	0.3%	0.204	0.0%	0.2%	0.999
Jaw Clench		(n=929)	(n=1,186)		(n=128)	(n=1,987)	
	Deviated	0.0%	0.2%	0.590	0.0%	0.1%	0.999
Smile		(n=929)	(n=1,186)		(n=128)	(n=1,987)	
	Abnormal	0.4%	0.6%	0.840	1.6%	0.5%	0.290
Palpebral Fissure		(n=929)	(n=1,186)		(n=128)	(n=1,987)	
	Abnormal	0.5%	1.2%	0.186	2.3%	0.8%	0.192
Balance		(n=929)	(n=1,185)		(n=127)	(n=1,987)	
	Abnormal	0.7%	0.7%	0.999	0.8%	0.7%	0.999
Speech		(n=929)	(n=1,186)		(n=128)	(n=1,987)	
	Abnormal	0.5%	0.8%	0.726	0.8%	0.7%	0.999
Tongue Position Relative		(n=929)	(n=1,186)		(n=128)	(n=1,987)	
to Midline	Deviated	0.0%	0.2%	0.590	0.0%	0.1%	0.999
Palate and Uvula		(n=929)	(n=1,186)		(n=128)	(n=1,987)	
Movement	Deviated	0.0%	0.1%	0.999	0.0%	0.1%	0.999
Cranial Nerve Index		(n=917)	(n=1,178)		(n=128)	(n=1,967)	
	Abnormal	4.4%	7.5%	0.004	10.2%	5.9%	0.075
Neck Range of Motion		(n=929)	(n=1,186)		(n=128)	(n=1,987)	
	Abnormal	9.9%	22.0%	<0.001	10.9%	17.1%	0.093
Pinprick		(n=910)	(n=1,097)		(n=124)	(n=1,883)	
	Abnormal	4.5%	7.6%	0.006	4.0%	6.3%	0.405
Light Touch		(n=910)	(n=1,097)		(n=124)	(n=1,883)	
	Abnormal	3.0%	5.1%	0.022	4.0%	4.1%	0.999
Muscle Status		(n=928)	(n=1,186)		(n=128)	(n=1,986)	
	Abnormal	2.7%	4.3%	0.064	3.1%	3.6%	0.960
Patellar Reflex		(n=928)	(n=1,183)		(n=128)	(n=1,983)	
	Abnormal	1.3%	4.0%	<0.001	6.3%	2.6%	0.030
Achilles Reflex		(n=925)	(n=1,184)		(n=128)	(n=1,981)	
	Abnormal	9.3%	22.8%	<0.001	20.3%	16.7%	0.343

Table F-3. Dependent Variable-Covariate Associations for the Neurology Assessment (Continued)

Dependent Variable	Level	Age: Born ≥1942	Age: Born <1942	Age: p-Value	Race: Black	Race: Non-Black	Race: p-Value
Biceps Reflex		(n=928)	(n=1,186)		(n=128)	(n=1,986)	
	Abnormal	1.0%	1.3%	0.668	0.8%	1.2%	0.999
Babinski Reflex		(n=929)	(n=1,183)		(n=127)	(n=1,985)	
	Abnormal	0.7%	1.3%	0.227	0.8%	1.0%	0.999
Polyneuropathy Severity		(n=907)	(n=1,096)		(n=123)	(n=1,880)	
Index	None/Mild	99.2%	97.1%	0.002	97.6%	98.1%	0.005
	Moderate	0.7%	2.6%		0.8%	1.8%	
	Severe	0.1%	0.4%		1.6%	0.2%	
Polyneuropathy		(n=907)	(n=1,097)		(n=124)	(n=1,880)	
Prevalence Index	Abnormal	8.8%	20.9%	<0.001	18.6%	15.2%	0.385
Multiple Polyneuropathy		(n=907)	(n=1,097)		(n=124)	(n=1,880)	
Index	Abnormal	1.8%	5.7%	<0.001	4.0%	3.9%	0.999
Confirmed		(n=905)	(n=1,082)		(n=121)	(n=1,866)	
Polyneuropathy Indicator	Abnormal	0.2%	1.5%	0.007	0.8%	0.9%	0.999
Tremor		(n=929)	(n=1,186)		(n=128)	(n=1,987)	
	Abnormal	6.0%	8.0%	0.095	6.3%	7.2%	0.821
Coordination		(n=928)	(n=1,185)		(n=127)	(n=1,986)	
	Abnormal	1.8%	2.8%	0.198	3.2%	2.3%	0.766
Romberg Sign		(n=929)	(n=1,185)		(n=127)	(n=1,987)	
	Abnormal	0.7%	0.7%	0.999	0.8%	0.7%	0.999
Gait		(n=929)	(n=1,186)		(n=128)	(n=1,987)	
	Abnormal	2.8%	6.8%	<0.001	4.7%	5.1%	0.999
Central Nervous System		(n=928)	(n=1,186)		(n=128)	(n=1,986)	
Index	Abnormal	8.7%	14.7%	<0.001	10.9%	12.1%	0.792

Table F-3. Dependent Variable-Covariate Associations for the Neurology Assessment (Continued)

Dependent Variable	Level	Occupation			p-Value
		Officer	Enlisted Flyer	Enlisted Groundcrew	
Inflammatory Diseases		(n=830)	(n=336)	(n=942)	
	Yes	0.2%	0.6%	0.4%	0.642
Hereditary and Degenerative Diseases		(n=833)	(n=338)	(n=944)	
	Yes	8.0%	11.2%	8.8%	0.217
Peripheral Disorders		(n=831)	(n=336)	(n=943)	
	Yes	20.3%	23.8%	19.1%	0.182
Other Neurological Disorders		(n=830)	(n=337)	(n=939)	
	Yes	8.1%	27.0%	24.1%	<0.001
Smell		(n=829)	(n=338)	(n=942)	
	Abnormal	1.8%	2.1%	1.8%	0.947
Visual Fields		(n=832)	(n=337)	(n=942)	
	Abnormal	0.1%	0.9%	0.3%	0.116
Light Reaction		(n=829)	(n=338)	(n=941)	
	Abnormal	0.4%	1.5%	0.5%	0.078
Ocular Movement		(n=833)	(n=338)	(n=944)	
	Abnormal	0.8%	1.5%	2.0%	0.122
Facial Sensation		(n=832)	(n=338)	(n=943)	
	Abnormal	0.2%	0.3%	0.1%	0.717
Jaw Clench		(n=833)	(n=338)	(n=944)	
	Deviated	0.2%	0.0%	0.0%	0.214
Smile		(n=833)	(n=338)	(n=944)	
	Abnormal	0.4%	0.3%	0.7%	0.442
Palpebral Fissure		(n=833)	(n=338)	(n=944)	
	Abnormal	0.8%	0.6%	1.1%	0.718
Balance		(n=833)	(n=337)	(n=944)	
	Abnormal	0.8%	0.3%	0.6%	0.578
Speech		(n=833)	(n=338)	(n=944)	
	Abnormal	0.4%	0.3%	1.1%	0.128
Tongue Position Relative to Midline		(n=833)	(n=338)	(n=944)	
	Deviated	0.2%	0.0%	0.0%	0.214
Palate and Uvula Movement		(n=833)	(n=338)	(n=944)	
	Deviated	0.1%	0.0%	0.0%	0.463
Cranial Nerve Index		(n=821)	(n=337)	(n=937)	
	Abnormal	5.2%	6.8%	6.6%	0.405
Neck Range of Motion		(n=833)	(n=338)	(n=944)	
	Abnormal	18.1%	20.7%	14.0%	0.006
Pinprick		(n=791)	(n=327)	(n=889)	
	Abnormal	5.3%	10.1%	5.5%	0.006
Light Touch		(n=791)	(n=327)	(n=889)	
	Abnormal	3.5%	6.7%	3.7%	0.036
Muscle Status		(n=833)	(n=338)	(n=943)	
	Abnormal	3.7%	5.0%	3.0%	0.211
Patellar Reflex		(n=833)	(n=337)	(n=941)	
	Abnormal	3.4%	2.4%	2.4%	0.443
Achilles Reflex		(n=831)	(n=337)	(n=941)	
	Abnormal	17.9%	19.9%	14.9%	0.064
Biceps Reflex		(n=833)	(n=338)	(n=943)	
	Abnormal	1.3%	1.2%	1.0%	0.765

Table F-3. Dependent Variable-Covariate Associations for the Neurology Assessment (Continued)

Dependent Variable	Level	Occupation: Officer	Occupation: Enlisted Flyer	Occupation: Enlisted Groundcrew	p-Value
Babinski Reflex		(n=832)	(n=336)	(n=944)	
	Abnormal	0.6%	1.2%	1.3%	0.337
Polyneuropathy Severity		(n=790)	(n=326)	(n=887)	
Index	None/Mild	98.0%	97.2%	98.4%	0.378
	Moderate	1.7%	2.8%	1.4%	
	Severe	0.4%	0.0%	0.2%	
Polyneuropathy Prevalence		(n=790)	(n=327)	(n=887)	
Index	Abnormal	16.5%	20.8%	12.5%	<0.001
Multiple Polyneuropathy		(n=790)	(n=327)	(n=887)	
Index	Abnormal	4.2%	6.7%	2.7%	0.006
Confirmed Polyneuropathy		(n=786)	(n=322)	(n=879)	
Indicator	Abnormal	1.0%	1.2%	0.7%	0.605
Tremor		(n=833)	(n=338)	(n=944)	
	Abnormal	6.1%	8.9%	7.4%	0.229
Coordination		(n=833)	(n=337)	(n=943)	
	Abnormal	2.2%	1.5%	2.9%	0.317
Romberg Sign		(n=833)	(n=337)	(n=944)	
	Abnormal	0.8%	0.3%	0.6%	0.578
Gait		(n=833)	(n=338)	(n=944)	
	Abnormal	5.4%	6.5%	4.2%	0.222
Central Nervous System		(n=833)	(n=338)	(n=943)	
Index	Abnormal	11.0%	15.4%	11.8%	0.110

Table F-3. Dependent Variable-Covariate Associations for the Neurology Assessment (Continued)

Dependent Variable	Level	Lifetime Alcohol History (drink-years) 0	>0–10	>10	p-Value
Inflammatory Diseases		(n=116)	(n=1,371)	(n=613)	
	Yes	0.0%	0.4%	0.5%	0.725
Hereditary and Degenerative Diseases		(n=118)	(n=1,374)	(n=615)	
	Yes	5.9%	8.4%	10.6%	0.154
Peripheral Disorders		(n=118)	(n=1,371)	(n=613)	
	Yes	24.6%	19.4%	21.9%	0.233
Other Neurological Disorders		(n=117)	(n=1,368)	(n=613)	
	Yes	18.8%	17.9%	18.9%	0.854
Smell		(n=117)	(n=1,369)	(n=615)	
	Abnormal	1.7%	2.1%	1.3%	0.514
Visual Fields		(n=118)	(n=1,372)	(n=613)	
	Abnormal	0.0%	0.4%	0.2%	0.502
Light Reaction		(n=118)	(n=1,369)	(n=613)	
	Abnormal	0.9%	0.7%	0.5%	0.861
Ocular Movement		(n=118)	(n=1,374)	(n=615)	
	Abnormal	2.5%	1.5%	1.3%	0.589
Facial Sensation		(n=118)	(n=1,372)	(n=615)	
	Abnormal	0.0%	0.1%	0.5%	0.129
Jaw Clench		(n=118)	(n=1,374)	(n=615)	
	Deviated	0.0%	0.1%	0.2%	0.787
Smile		(n=118)	(n=1,374)	(n=615)	
	Abnormal	0.9%	0.4%	0.8%	0.386
Palpebral Fissure		(n=118)	(n=1,374)	(n=615)	
	Abnormal	1.7%	0.6%	1.3%	0.163
Balance		(n=118)	(n=1,373)	(n=615)	
	Abnormal	0.9%	0.5%	1.0%	0.482
Speech		(n=118)	(n=1,374)	(n=615)	
	Abnormal	0.0%	0.6%	1.0%	0.400
Tongue Position Relative to Midline		(n=118)	(n=1,374)	(n=615)	
	Deviated	0.0%	0.1%	0.2%	0.787
Palate and Uvula Movement		(n=118)	(n=1,374)	(n=615)	
	Deviated	0.0%	0.0%	0.2%	0.297
Cranial Nerve Index		(n=116)	(n=1,356)	(n=615)	
	Abnormal	7.8%	5.5%	6.8%	0.387
Neck Range of Motion		(n=118)	(n=1,374)	(n=615)	
	Abnormal	15.3%	15.8%	19.2%	0.156
Pinprick		(n=107)	(n=1,309)	(n=583)	
	Abnormal	9.4%	5.4%	7.2%	0.122
Light Touch		(n=107)	(n=1,309)	(n=583)	
	Abnormal	4.7%	3.5%	5.3%	0.180
Muscle Status		(n=118)	(n=1,373)	(n=615)	
	Abnormal	5.1%	3.1%	4.4%	0.257
Patellar Reflex		(n=118)	(n=1,370)	(n=615)	
	Abnormal	5.1%	2.6%	2.8%	0.300
Achilles Reflex		(n=118)	(n=1,368)	(n=615)	
	Abnormal	18.6%	15.4%	20.2%	0.027

Table F-3. Dependent Variable-Covariate Associations for the Neurology Assessment (Continued)

Dependent Variable	Level	Lifetime Alcohol History (drink-years) 0	>0–10	>10	p-Value
Biceps Reflex		(n=118)	(n=1,373)	(n=615)	
	Abnormal	1.7%	1.2%	0.8%	0.635
Babinski Reflex		(n=118)	(n=1,371)	(n=615)	
	Abnormal	2.5%	0.9%	0.8%	0.184
Polyneuropathy Severity Index		(n=107)	(n=1,305)	(n=583)	
	None/Mild	99.1%	98.3%	97.3%	0.088
	Moderate	0.0%	1.6%	2.2%	
	Severe	0.9%	0.1%	0.5%	
Polyneuropathy Prevalence Index		(n=107)	(n=1,306)	(n=583)	
	Abnormal	13.1%	13.5%	20.2%	<0.001
Multiple Polyneuropathy Index		(n=107)	(n=1,306)	(n=583)	
	Abnormal	3.7%	3.2%	5.5%	0.062
Confirmed Polyneuropathy Indicator		(n=105)	(n=1,299)	(n=575)	
	Abnormal	1.0%	0.9%	1.0%	0.917
Tremor		(n=118)	(n=1,374)	(n=615)	
	Abnormal	3.4%	7.0%	8.3%	0.152
Coordination		(n=118)	(n=1,372)	(n=615)	
	Abnormal	0.9%	2.0%	3.4%	0.095
Romberg Sign		(n=118)	(n=1,373)	(n=615)	
	Abnormal	0.9%	0.5%	1.0%	0.482
Gait		(n=118)	(n=1,374)	(n=615)	
	Abnormal	5.1%	4.9%	5.5%	0.829
Central Nervous System Index		(n=118)	(n=1,373)	(n=615)	
	Abnormal	9.3%	11.4%	14.2%	0.146

Table F-3. Dependent Variable-Covariate Associations for the Neurology Assessment (Continued)

Dependent Variable	Level	Insecticide Exposure			Industrial Chemical Exposure		
		No	Yes	p-Value	No	Yes	p-Value
Inflammatory Diseases		(n=619)	(n=1,489)		(n=796)	(n=1,312)	
	Yes	0.7%	0.3%	0.371	0.1%	0.5%	0.266
Hereditary and Degenerative		(n=621)	(n=1,494)		(n=799)	(n=1,316)	
Diseases	Yes	7.1%	9.6%	0.073	7.0%	10.0%	0.022
Peripheral Disorders		(n=621)	(n=1,489)		(n=798)	(n=1,312)	
	Yes	16.9%	21.8%	0.014	20.2%	20.4%	0.934
Other Neurological		(n=620)	(n=1,486)		(n=797)	(n=1,309)	
Disorders	Yes	15.7%	19.3%	0.054	13.3%	21.2%	<0.001
Smell		(n=621)	(n=1,488)		(n=798)	(n=1,311)	
	Abnormal	1.5%	2.0%	0.482	1.9%	1.8%	0.999
Visual Fields		(n=620)	(n=1,491)		(n=798)	(n=1,313)	
	Abnormal	0.5%	0.3%	0.712	0.5%	0.2%	0.505
Light Reaction		(n=621)	(n=1,487)		(n=797)	(n=1,311)	
	Abnormal	1.1%	0.4%	0.103	0.8%	0.5%	0.737
Ocular Movement		(n=621)	(n=1,494)		(n=799)	(n=1,316)	
	Abnormal	1.3%	1.5%	0.811	1.4%	1.5%	0.937
Facial Sensation		(n=621)	(n=1,492)		(n=798)	(n=1,315)	
	Abnormal	0.0%	0.3%	0.458	0.1%	0.2%	0.991
Jaw Clench		(n=621)	(n=1,494)		(n=799)	(n=1,316)	
	Deviated	0.0%	0.1%	0.892	0.1%	0.1%	0.999
Smile		(n=621)	(n=1,494)		(n=799)	(n=1,316)	
	Abnormal	0.3%	0.6%	0.628	0.4%	0.6%	0.683
Palpebral Fissure		(n=621)	(n=1,494)		(n=799)	(n=1,316)	
	Abnormal	0.5%	1.1%	0.293	1.1%	0.8%	0.530
Balance		(n=620)	(n=1,494)		(n=798)	(n=1,316)	
	Abnormal	0.5%	0.7%	0.721	0.5%	0.8%	0.664
Speech		(n=621)	(n=1,494)		(n=799)	(n=1,316)	
	Abnormal	0.8%	0.6%	0.819	0.8%	0.6%	0.907
Tongue Position Relative to		(n=621)	(n=1,494)		(n=799)	(n=1,316)	
Midline	Deviated	0.0%	0.1%	0.892	0.1%	0.1%	0.999
Palate and Uvula Movement		(n=621)	(n=1,494)		(n=799)	(n=1,316)	
	Deviated	0.0%	0.1%	0.999	0.0%	0.1%	0.999
Cranial Nerve Index		(n=617)	(n=1,478)		(n=792)	(n=1,303)	
	Abnormal	5.4%	6.4%	0.401	6.4%	5.9%	0.691
Neck Range of Motion		(n=621)	(n=1,494)		(n=799)	(n=1,316)	
	Abnormal	15.3%	17.3%	0.297	17.8%	16.0%	0.327
Pinprick		(n=597)	(n=1,410)		(n=751)	(n=1,256)	
	Abnormal	5.7%	6.4%	0.629	6.3%	6.1%	0.985
Light Touch		(n=597)	(n=1,410)		(n=751)	(n=1,256)	
	Abnormal	3.5%	4.4%	0.434	4.7%	3.8%	0.425
Muscle Status		(n=621)	(n=1,493)		(n=799)	(n=1,315)	
	Abnormal	2.4%	4.1%	0.080	3.4%	3.7%	0.768
Patellar Reflex		(n=620)	(n=1,491)		(n=798)	(n=1,313)	
	Abnormal	2.7%	2.8%	0.999	2.6%	2.9%	0.827
Achilles Reflex		(n=619)	(n=1,490)		(n=796)	(n=1,313)	
	Abnormal	15.8%	17.3%	0.445	17.8%	16.3%	0.392
Biceps Reflex		(n=620)	(n=1,494)		(n=798)	(n=1,316)	
	Abnormal	1.1%	1.1%	0.999	1.5%	0.9%	0.301

Table F-3. Dependent Variable-Covariate Associations for the Neurology Assessment (Continued)

Dependent Variable	Level	Insecticide Exposure			Industrial Chemical Exposure		
		No	Yes	p-Value	No	Yes	p-Value
Babinski Reflex		(n=619)	(n=1,493)		(n=797)	(n=1,315)	
	Abnormal	1.1%	0.9%	0.868	0.6%	1.2%	0.273
Polyneuropathy Severity		(n=596)	(n=1,407)		(n=749)	(n=1,254)	
Index	None/Mild	98.7%	97.8%	0.443	98.0%	98.1%	0.561
	Moderate	1.2%	1.9%		1.6%	1.8%	
	Severe	0.2%	0.3%		0.4%	0.2%	
Polyneuropathy Prevalence		(n=597)	(n=1,407)		(n=750)	(n=1,254)	
Index	Abnormal	14.1%	16.0%	0.307	16.7%	14.7%	0.258
Multiple Polyneuropathy		(n=597)	(n=1,407)		(n=750)	(n=1,254)	
Index	Abnormal	3.7%	4.1%	0.795	4.4%	3.7%	0.486
Confirmed Polyneuropathy		(n=591)	(n=1,396)		(n=744)	(n=1,243)	
Indicator	Abnormal	0.5%	1.1%	0.337	0.8%	1.0%	0.907
Tremor		(n=621)	(n=1,494)		(n=799)	(n=1,316)	
	Abnormal	4.5%	8.2%	0.003	5.0%	8.4%	0.004
Coordination		(n=619)	(n=1,494)		(n=797)	(n=1,316)	
	Abnormal	1.6%	2.7%	0.192	2.3%	2.4%	0.915
Romberg Sign		(n=620)	(n=1,494)		(n=798)	(n=1,316)	
	Abnormal	0.5%	0.7%	0.721	0.5%	0.8%	0.664
Gait		(n=621)	(n=1,494)		(n=799)	(n=1,316)	
	Abnormal	3.9%	5.6%	0.132	5.0%	5.1%	0.999
Central Nervous		(n=620)	(n=1,494)		(n=798)	(n=1,316)	
System Index	Abnormal	8.2%	13.7%	<0.001	9.9%	13.4%	0.021

Table F-3. Dependent Variable-Covariate Associations for the Neurology Assessment (Continued)

Dependent Variable	Level	Degreasing Chemical Exposure: No	Degreasing Chemical Exposure: Yes	p-Value	Diabetic Class: Normal	Diabetic Class: Impaired	Diabetic Class: Diabetic	p-Value
Inflammatory Diseases	Yes	(n=751) 0.1%	(n=1,357) 0.5%	0.318	(n=1,453) 0.5%	(n=273) 0.0%	(n=355) 0.3%	0.470
Hereditary and Degenerative Diseases	Yes	(n=752) 9.2%	(n=1,363) 8.7%	0.792	(n=1,458) 8.0%	(n=273) 10.6%	(n=357) 10.9%	0.123
Peripheral Disorders	Yes	(n=752) 18.5%	(n=1,358) 21.4%	0.130	(n=1,454) 17.5%	(n=273) 18.7%	(n=356) 33.4%	<0.001
Other Neurological Disorders	Yes	(n=748) 13.9%	(n=1,358) 20.6%	<0.001	(n=1,451) 16.0%	(n=272) 21.3%	(n=356) 23.9%	<0.001
Smell	Abnormal	(n=750) 2.0%	(n=1,359) 1.8%	0.831	(n=1,454) 1.5%	(n=273) 2.9%	(n=355) 1.7%	0.257
Visual Fields	Abnormal	(n=751) 0.1%	(n=1,360) 0.4%	0.434	(n=1,456) 0.3%	(n=273) 0.4%	(n=355) 0.6%	0.698
Light Reaction	Abnormal	(n=750) 0.7%	(n=1,358) 0.6%	0.999	(n=1,453) 0.6%	(n=273) 0.4%	(n=355) 1.1%	0.394
Ocular Movement	Abnormal	(n=752) 1.2%	(n=1,363) 1.6%	0.565	(n=1,458) 1.3%	(n=273) 1.5%	(n=357) 2.2%	0.422
Facial Sensation	Abnormal	(n=750) 0.1%	(n=1,363) 0.2%	0.999	(n=1,457) 0.2%	(n=272) 0.0%	(n=357) 0.3%	0.711
Jaw Clench	Deviated	(n=752) 0.1%	(n=1,363) 0.1%	0.999	(n=1,458) 0.0%	(n=273) 0.4%	(n=357) 0.3%	0.093
Smile	Abnormal	(n=752) 0.3%	(n=1,363) 0.7%	0.373	(n=1,458) 0.4%	(n=273) 0.0%	(n=357) 1.4%	0.030
Palpebral Fissure	Abnormal	(n=752) 0.4%	(n=1,363) 1.2%	0.117	(n=1,458) 0.8%	(n=273) 0.0%	(n=357) 2.2%	0.007
Balance	Abnormal	(n=752) 0.8%	(n=1,362) 0.6%	0.771	(n=1,458) 0.5%	(n=273) 0.4%	(n=356) 1.7%	0.036
Speech	Abnormal	(n=752) 0.5%	(n=1,363) 0.7%	0.789	(n=1,458) 0.6%	(n=273) 0.7%	(n=357) 0.8%	0.890
Tongue Position Relative to Midline	Deviated	(n=752) 0.1%	(n=1,363) 0.1%	0.999	(n=1,458) 0.0%	(n=273) 0.4%	(n=357) 0.3%	0.093
Palate and Uvula Movement	Deviated	(n=752) 0.0%	(n=1,363) 0.1%	0.999	(n=1,458) 0.0%	(n=273) 0.0%	(n=357) 0.3%	0.088
Cranial Nerve Index	Abnormal	(n=743) 5.8%	(n=1,352) 6.3%	0.718	(n=1,443) 5.2%	(n=271) 6.3%	(n=354) 9.3%	0.014
Neck Range of Motion	Abnormal	(n=752) 17.8%	(n=1,363) 16.1%	0.330	(n=1,458) 15.6%	(n=273) 15.4%	(n=357) 21.6%	0.022
Pinprick	Abnormal	(n=712) 6.0%	(n=1,295) 6.3%	0.924	(n=1,408) 4.1%	(n=251) 4.0%	(n=322) 16.8%	<0.001
Light Touch	Abnormal	(n=712) 4.1%	(n=1,295) 4.2%	0.999	(n=1,408) 3.0%	(n=251) 2.0%	(n=322) 10.6%	<0.001
Muscle Status	Abnormal	(n=752) 3.9%	(n=1,362) 3.5%	0.721	(n=1,457) 3.3%	(n=273) 2.6%	(n=357) 5.6%	0.068
Patellar Reflex	Abnormal	(n=751) 2.8%	(n=1,360) 2.8%	0.999	(n=1,455) 1.8%	(n=273) 2.6%	(n=356) 7.3%	<0.001
Achilles Reflex	Abnormal	(n=748) 18.9%	(n=1,361) 15.8%	0.084	(n=1,453) 13.4%	(n=272) 16.2%	(n=357) 31.9%	<0.001

Table F-3. Dependent Variable-Covariate Associations for the Neurology Assessment (Continued)

Dependent Variable	Level	Degreasing Chemical Exposure			Diabetic Class			
		No	Yes	p-Value	Normal	Impaired	Diabetic	p-Value
Biceps Reflex		(n=751)	(n=1,363)		(n=1,458)	(n=272)	(n=357)	
	Abnormal	1.3%	1.0%	0.676	0.7%	1.8%	2.5%	0.007
Babinski Reflex		(n=751)	(n=1,361)		(n=1,456)	(n=273)	(n=356)	
	Abnormal	0.9%	1.0%	0.999	0.9%	1.1%	1.4%	0.678
Polyneuropathy		(n=710)	(n=1,293)		(n=1,405)	(n=251)	(n=321)	
Severity Index	None/Mild	98.0%	98.0%	0.482	98.9%	99.6%	93.2%	<0.001
	Moderate	1.6%	1.8%		0.9%	0.4%	5.9%	
	Severe	0.4%	0.2%		0.1%	0.0%	0.9%	
Polyneuropathy		(n=710)	(n=1,294)		(n=1,405)	(n=251)	(n=322)	
Prevalence Index	Abnormal	16.5%	14.8%	0.364	12.0%	12.4%	32.9%	<0.001
Multiple		(n=710)	(n=1,294)		(n=1,405)	(n=251)	(n=322)	
Polyneuropathy Index	Abnormal	3.9%	3.9%	0.999	2.4%	1.2%	12.7%	<0.001
Confirmed		(n=704)	(n=1,283)		(n=1,397)	(n=251)	(n=313)	
Polyneuropathy Indicator	Abnormal	0.7%	1.0%	0.664	0.6%	0.0%	2.9%	<0.001
Tremor		(n=752)	(n=1,363)		(n=1,458)	(n=273)	(n=357)	
	Abnormal	6.4%	7.6%	0.360	7.2%	7.3%	6.4%	0.870
Coordination		(n=751)	(n=1,362)		(n=1,458)	(n=272)	(n=356)	
	Abnormal	2.7%	2.2%	0.605	1.9%	2.2%	4.5%	0.013
Romberg Sign		(n=752)	(n=1,362)		(n=1,458)	(n=273)	(n=356)	
	Abnormal	0.8%	0.6%	0.771	0.5%	0.4%	1.7%	0.036
Gait		(n=752)	(n=1,363)		(n=1,458)	(n=273)	(n=357)	
	Abnormal	4.9%	5.1%	0.910	3.9%	5.1%	9.2%	<0.001
Central Nervous		(n=751)	(n=1,363)		(n=1,458)	(n=272)	(n=357)	
System Index	Abnormal	11.2%	12.6%	0.396	11.0%	12.9%	15.4%	0.062

Dependent Variable	Level	Composite Exposure to Heavy Metals			Worked With Vibrating Power Equipment or Tools		
		No	Yes	p-Value	No	Yes	p-Value
Confirmed Polyneuropathy		(n=1,714)	(n=272)		(n=1,446)	(n=538)	
Indicator	Abnormal	0.8%	1.5%	0.476	1.0%	0.7%	0.839

Table F-4. Dependent Variable-Covariate Associations for the Psychology Assessment

Dependent Variable	Level	Age: Born ≥1942	Age: Born <1942	Age: p-Value	Race: Black	Race: Non-Black	Race: p-Value
Psychoses		(n=929)	(n=1,187)		(n=128)	(n=1,988)	
	Yes	4.2%	3.6%	0.571	3.9%	3.9%	0.999
Alcohol Dependence		(n=928)	(n=1,187)		(n=127)	(n=1,988)	
	Yes	6.6%	7.1%	0.713	10.2%	6.6%	0.169
Drug Dependence		(n=929)	(n=1,187)		(n=128)	(n=1,988)	
	Yes	0.5%	0.1%	0.124	1.6%	0.2%	0.051
Anxiety		(n=926)	(n=1,183)		(n=128)	(n=1,981)	
	Yes	28.3%	25.7%	0.198	25.0%	27.0%	0.703
Other Neuroses		(n=921)	(n=1,174)		(n=127)	(n=1,968)	
	Yes	54.8%	53.0%	0.424	55.9%	53.7%	0.689
SCL-90-R Anxiety		(n=929)	(n=1,186)		(n=128)	(n=1,987)	
	High	11.8%	9.4%	0.087	11.7%	10.4%	0.751
SCL-90-R Depression		(n=929)	(n=1,186)		(n=128)	(n=1,987)	
	High	16.8%	13.5%	0.040	14.1%	15.0%	0.873
SCL-90-R Hostility		(n=929)	(n=1,186)		(n=128)	(n=1,987)	
	High	9.6%	7.0%	0.038	8.6%	8.1%	0.976
SCL-90-R Interpersonal		(n=929)	(n=1,186)		(n=128)	(n=1,987)	
Sensitivity	High	17.3%	13.6%	0.020	16.4%	15.2%	0.797
SCL-90-R Obsessive-		(n=929)	(n=1,186)		(n=128)	(n=1,987)	
Compulsive Behavior	High	15.5%	15.4%	0.970	14.1%	15.5%	0.756
SCL-90-R Paranoid		(n=929)	(n=1,186)		(n=128)	(n=1,987)	
Ideation	High	9.0%	5.2%	0.001	10.9%	6.6%	0.093
SCL-90-R Phobic		(n=929)	(n=1,186)		(n=128)	(n=1,987)	
Anxiety	High	12.4%	8.5%	0.005	14.8%	9.9%	0.102
SCL-90-R Psychoticism		(n=929)	(n=1,186)		(n=128)	(n=1,987)	
	High	15.6%	12.1%	0.025	18.8%	13.3%	0.111
SCL-90-R Somatization		(n=929)	(n=1,186)		(n=128)	(n=1,987)	
	High	17.2%	15.5%	0.319	20.3%	16.0%	0.247
SCL-90-R Global		(n=929)	(n=1,186)		(n=128)	(n=1,987)	
Severity Index	High	16.6%	13.4%	0.048	15.6%	14.8%	0.886
SCL-90-R Positive		(n=929)	(n=1,186)		(n=128)	(n=1,987)	
Symptom Total	High	17.6%	14.6%	0.074	18.0%	15.8%	0.589
SCL-90-R Positive		(n=929)	(n=1,186)		(n=128)	(n=1,987)	
Symptom Distress Index	High	8.4%	6.3%	0.082	8.6%	7.2%	0.662

Table F-4. Dependent Variable-Covariate Associations for the Psychology Assessment (Continued)

Dependent Variable	Level	Occupation			
		Officer	Enlisted Flyer	Enlisted Groundcrew	p-Value
Psychoses		(n=834)	(n=338)	(n=944)	
	Yes	2.5%	5.0%	4.7%	0.032
Alcohol Dependence		(n=834)	(n=338)	(n=943)	
	Yes	4.9%	8.9%	7.9%	0.014
Drug Dependence		(n=834)	(n=338)	(n=944)	
	Yes	0.1%	0.0%	0.5%	0.152
Anxiety		(n=833)	(n=337)	(n=939)	
	Yes	17.3%	30.9%	33.9%	0.001
Other Neuroses		(n=829)	(n=334)	(n=932)	
	Yes	43.7%	61.4%	60.1%	0.001
SCL-90-R Anxiety		(n=834)	(n=337)	(n=944)	
	High	5.0%	13.4%	14.3%	0.001
SCL-90-R Depression		(n=834)	(n=337)	(n=944)	
	High	9.0%	17.5%	19.3%	0.001
SCL-90-R Hostility		(n=834)	(n=337)	(n=944)	
	High	4.1%	9.5%	11.2%	0.001
SCL-90-R Interpersonal		(n=834)	(n=337)	(n=944)	
Sensitivity	High	7.8%	19.0%	20.4%	0.001
SCL-90-R Obsessive-		(n=834)	(n=337)	(n=944)	
Compulsive Behavior	High	9.2%	20.5%	19.1%	0.001
SCL-90-R Paranoid		(n=834)	(n=337)	(n=944)	
Ideation	High	2.8%	7.4%	10.4%	0.001
SCL-90-R Phobic		(n=834)	(n=337)	(n=944)	
Anxiety	High	4.6%	12.5%	14.4%	0.001
SCL-90-R Psychoticism		(n=834)	(n=337)	(n=944)	
	High	7.9%	14.8%	18.3%	0.001
SCL-90-R Somatization		(n=834)	(n=337)	(n=944)	
	High	7.3%	25.2%	21.0%	0.001
SCL-90-R Global		(n=834)	(n=337)	(n=944)	
Severity Index	High	7.2%	18.7%	20.1%	0.001
SCL-90-R Positive		(n=834)	(n=337)	(n=944)	
Symptom Total	High	8.5%	20.2%	20.9%	0.001
SCL-90-R Positive		(n=834)	(n=337)	(n=944)	
Symptom Distress Index	High	3.7%	9.5%	9.5%	0.001

Table F-4. Dependent Variable-Covariate Associations for the Psychology Assessment (Continued)

Dependent Variable	Level	Education: College	Education: High School	p-Value
Psychoses		(n=1,139)	(n=976)	
	Yes	3.3%	4.6%	0.132
Alcohol Dependence		(n=1,139)	(n=975)	
	Yes	6.0%	7.9%	0.097
Drug Dependence		(n=1,139)	(n=976)	
	Yes	0.4%	0.2%	0.826
Anxiety		(n=1,136)	(n=972)	
	Yes	23.1%	31.3%	0.001
Other Neuroses		(n=1,133)	(n=961)	
	Yes	47.8%	60.9%	0.001
SCL-90-R Anxiety		(n=1,139)	(n=975)	
	High	7.5%	14.1%	0.001
SCL-90-R Depression		(n=1,139)	(n=975)	
	High	11.2%	19.4%	0.001
SCL-90-R Hostility		(n=1,139)	(n=975)	
	High	5.4%	11.3%	0.001
SCL-90-R Interpersonal		(n=1,139)	(n=975)	
Sensitivity	High	10.8%	20.4%	0.001
SCL-90-R Obsessive-		(n=1,139)	(n=975)	
Compulsive Behavior	High	11.8%	19.7%	0.001
SCL-90-R Paranoid		(n=1,139)	(n=975)	
Ideation	High	4.5%	9.7%	0.001
SCL-90-R Phobic		(n=1,139)	(n=975)	
Anxiety	High	6.6%	14.5%	0.001
SCL-90-R Psychoticism		(n=1,139)	(n=975)	
	High	10.7%	17.1%	0.001
SCL-90-R Somatization		(n=1,139)	(n=975)	
	High	11.2%	22.3%	0.001
SCL-90-R Global		(n=1,139)	(n=975)	
Severity Index	High	11.1%	19.2%	0.001
SCL-90-R Positive		(n=1,139)	(n=975)	
Symptom Total	High	11.7%	20.8%	0.001
SCL-90-R Positive		(n=1,139)	(n=975)	
Symptom Distress Index	High	5.3%	9.5%	0.001

Table F-4. Dependent Variable-Covariate Associations for the Psychology Assessment (Continued)

Dependent Variable	Level	Current Alcohol Use (drinks/day) 0–1	>1–4	>4	p-Value
Alcohol Dependence		--	--	--	--
Drug Dependence		--	--	--	--
Anxiety		--	--	--	--
Other Neuroses		--	--	--	--
SCL-90-R Anxiety		(n=1,694)	(n=370)	(n=50)	
	High	10.6%	8.9%	20.0%	0.055
SCL-90-R Depression		(n=1,694)	(n=370)	(n=50)	
	High	14.9%	13.2%	28.0%	0.023
SCL-90-R Hostility		(n=1,694)	(n=370)	(n=50)	
	High	8.2%	6.8%	18.0%	0.024
SCL-90-R Interpersonal		(n=1,694)	(n=370)	(n=50)	
Sensitivity	High	15.8%	11.6%	22.0%	0.051
SCL-90-R Obsessive-		(n=1,694)	(n=370)	(n=50)	
Compulsive Behavior	High	15.5%	13.8%	26.0%	0.080
SCL-90-R Paranoid		(n=1,694)	(n=370)	(n=50)	
Ideation	High	7.0%	6.0%	12.0%	0.278
SCL-90-R Phobic		(n=1,694)	(n=370)	(n=50)	
Anxiety	High	10.0%	10.5%	14.0%	0.643
SCL-90-R Psychoticism		(n=1,694)	(n=370)	(n=50)	
	High	13.5%	13.0%	24.0%	0.095
SCL-90-R Somatization		(n=1,694)	(n=370)	(n=50)	
	High	17.1%	11.9%	20.0%	0.037
SCL-90-R Global		(n=1,694)	(n=370)	(n=50)	
Severity Index	High	14.9%	12.7%	28.0%	0.017
SCL-90-R Positive		(n=1,694)	(n=370)	(n=50)	
Symptom Total	High	16.1%	14.1%	22.0%	0.302
SCL-90-R Positive		(n=1,694)	(n=370)	(n=50)	
Symptom Distress Index	High	7.7%	4.3%	12.0%	0.030

Table F-4. Dependent Variable-Covariate Associations for the Psychology Assessment (Continued)

Dependent Variable	Level	Lifetime Alcohol History (drink-years) 0	>0–10	>10	p-Value
Psychoses		(n=118)	(n=1,375)	(n=615)	
	Yes	3.4%	3.3%	5.4%	0.080
Alcohol Dependence		--	--	--	--
Drug Dependence		(n=118)	(n=1,375)	(n=615)	
	Yes	0.0%	0.2%	0.5%	0.485
Anxiety		(n=118)	(n=1,371)	(n=612)	
	Yes	27.1%	26.4%	27.6%	0.851
Other Neuroses		(n=118)	(n=1,364)	(n=605)	
	Yes	50.9%	50.2%	62.8%	0.001
SCL-90-R Anxiety		(n=118)	(n=1,374)	(n=615)	
	High	11.0%	9.1%	13.7%	0.009
SCL-90-R Depression		(n=118)	(n=1,374)	(n=615)	
	High	17.0%	12.9%	19.4%	0.001
SCL-90-R Hostility		(n=118)	(n=1,374)	(n=615)	
	High	3.4%	7.4%	10.9%	0.004
SCL-90-R Interpersonal		(n=118)	(n=1,374)	(n=615)	
Sensitivity	High	14.4%	14.1%	18.2%	0.056
SCL-90-R Obsessive-		(n=118)	(n=1,374)	(n=615)	
Compulsive Behavior	High	14.4%	13.6%	19.8%	0.002
SCL-90-R Paranoid		(n=118)	(n=1,374)	(n=615)	
Ideation	High	5.1%	6.3%	8.8%	0.089
SCL-90-R Phobic		(n=118)	(n=1,374)	(n=615)	
Anxiety	High	5.9%	9.4%	13.0%	0.014
SCL-90-R Psychoticism		(n=118)	(n=1,374)	(n=615)	
	High	11.9%	12.2%	17.6%	0.004
SCL-90-R Somatization		(n=118)	(n=1,374)	(n=615)	
	High	12.7%	15.6%	18.7%	0.121
SCL-90-R Global		(n=118)	(n=1,374)	(n=615)	
Severity Index	High	15.3%	12.7%	19.5%	0.001
SCL-90-R Positive		(n=118)	(n=1,374)	(n=615)	
Symptom Total	High	16.1%	14.0%	20.3%	0.002
SCL-90-R Positive		(n=118)	(n=1,374)	(n=615)	
Symptom Distress Index	High	7.6%	7.1%	7.6%	0.887

Table F-4 Dependent Variable-Covariate Associations for the Psychology Assessment (Continued)

Dependent Variable	Level	Current Total Household Income ≤$65,000	>$65,000	p-Value	Current Employment Yes	No	p-Value
Psychoses		(n=1,062)	(n=1,030)		(n=1,385)	(n=730)	
	Yes	5.0%	2.7%	0.010	3.3%	5.1%	0.052
Alcohol Dependence		(n=1,061)	(n=1,030)		(n=1,384)	(n=730)	
	Yes	8.8%	5.0%	0.001	6.0%	8.5%	0.039
Drug Dependence		(n=1,062)	(n=1,030)		(n=1,385)	(n=730)	
	Yes	0.4%	0.2%	0.710	0.4%	0.0%	0.177
Anxiety		(n=1,059)	(n=1,027)		(n=1,381)	(n=727)	
	Yes	32.8%	20.9%	0.001	26.5%	27.5%	0.657
Other Neuroses		(n=1,048)	(n=1,023)		(n=1,373)	(n=721)	
	Yes	61.6%	45.7%	0.001	52.4%	56.3%	0.101
SCL-90-R Anxiety		(n=1,062)	(n=1,029)		(n=1,384)	(n=730)	
	High	14.5%	6.2%	0.001	10.3%	11.0%	0.672
SCL-90-R Depression		(n=1,062)	(n=1,029)		(n=1,384)	(n=730)	
	High	19.7%	9.8%	0.001	14.7%	15.3%	0.760
SCL-90-R Hostility		(n=1,062)	(n=1,029)		(n=1,384)	(n=730)	
	High	10.6%	5.4%	0.001	8.2%	8.0%	0.881
SCL-90-R Interpersonal		(n=1,062)	(n=1,029)		(n=1,384)	(n=730)	
Sensitivity	High	20.0%	10.2%	0.001	15.2%	15.3%	0.969
SCL-90-R Obsessive-		(n=1,062)	(n=1,029)		(n=1,384)	(n=730)	
Compulsive Behavior	High	20.8%	9.8%	0.001	14.3%	17.5%	0.059
SCL-90-R Paranoid		(n=1,062)	(n=1,029)		(n=1,384)	(n=730)	
Ideation	High	9.7%	3.8%	0.001	7.4%	6.0%	0.286
SCL-90-R Phobic		(n=1,062)	(n=1,029)		(n=1,384)	(n=730)	
Anxiety	High	14.1%	5.9%	0.001	9.5%	11.5%	0.178
SCL-90-R Psychoticism		(n=1,062)	(n=1,029)		(n=1,384)	(n=730)	
	High	18.1%	8.9%	0.001	13.5%	14.0%	0.821
SCL-90-R Somatization		(n=1,062)	(n=1,029)		(n=1,384)	(n=730)	
	High	21.8%	10.5%	0.001	14.9%	18.9%	0.020
SCL-90-R Global		(n=1,062)	(n=1,029)		(n=1,384)	(n=730)	
Severity Index	High	19.9%	9.5%	0.001	14.2%	15.9%	0.340
SCL-90-R Positive		(n=1,062)	(n=1,029)		(n=1,384)	(n=730)	
Symptom Total	High	21.0%	10.5%	0.001	15.5%	16.7%	0.493
SCL-90-R Positive		(n=1,062)	(n=1,029)		(n=1,384)	(n=730)	
Symptom Distress Index	High	8.7%	5.7%	0.012	6.8%	8.1%	0.317

Table F-4 Dependent Variable-Covariate Associations for the Psychology Assessment (Continued)

Dependent Variable	Level	Current Marital Status: Married	Not Married	p-Value	Current Parental Status: Child<18 Years Old	No Child<18 Years Old	p-Value
Psychoses		(n=1,745)	(n=370)		(n=290)	(n=1,825)	
	Yes	3.0%	7.8%	0.001	3.5%	4.0%	0.808
Alcohol Dependence		(n=1,745)	(n=369)		(n=290)	(n=1,824)	
	Yes	5.3%	14.4%	0.001	3.1%	7.5%	0.009
Drug Dependence		(n=1,745)	(n=370)		(n=290)	(n=1,825)	
	Yes	0.1%	1.1%	0.008	0.3%	0.3%	0.999
Anxiety		(n=1,740)	(n=368)		(n=290)	(n=1,818)	
	Yes	25.3%	34.0%	0.001	23.8%	27.3%	0.233
Other Neuroses		(n=1,730)	(n=364)		(n=288)	(n=1,806)	
	Yes	51.9%	62.9%	0.001	56.3%	53.4%	0.398
SCL-90-R Anxiety		(n=1,745)	(n=369)		(n=290)	(n=1,824)	
	High	9.8%	13.8%	0.028	10.7%	10.5%	0.992
SCL-90-R Depression		(n=1,745)	(n=369)		(n=290)	(n=1,824)	
	High	13.8%	20.3%	0.002	16.6%	14.7%	0.462
SCL-90-R Hostility		(n=1,745)	(n=369)		(n=290)	(n=1,824)	
	High	8.5%	6.5%	0.247	9.3%	8.0%	0.502
SCL-90-R Interpersonal		(n=1,745)	(n=369)		(n=290)	(n=1,824)	
Sensitivity	High	14.4%	19.2%	0.023	14.5%	15.4%	0.769
SCL-90-R Obsessive-		(n=1,745)	(n=369)		(n=290)	(n=1,824)	
Compulsive Behavior	High	14.8%	18.4%	0.093	13.8%	15.7%	0.460
SCL-90-R Paranoid		(n=1,745)	(n=369)		(n=290)	(n=1,824)	
Ideation	High	6.1%	10.8%	0.002	7.9%	6.7%	0.538
SCL-90-R Phobic		(n=1,745)	(n=369)		(n=290)	(n=1,824)	
Anxiety	High	9.6%	13.0%	0.064	8.6%	10.5%	0.389
SCL-90-R Psychoticism		(n=1,745)	(n=369)		(n=290)	(n=1,824)	
	High	12.5%	19.2%	0.001	14.8%	13.5%	0.599
SCL-90-R Somatization		(n=1,745)	(n=369)		(n=290)	(n=1,824)	
	High	15.6%	19.5%	0.075	14.8%	16.5%	0.527
SCL-90-R Global		(n=1,745)	(n=369)		(n=290)	(n=1,824)	
Severity Index	High	13.9%	19.0%	0.016	14.5%	14.9%	0.938
SCL-90-R Positive		(n=1,745)	(n=369)		(n=290)	(n=1,824)	
Symptom Total	High	15.2%	19.2%	0.063	16.2%	15.8%	0.944
SCL-90-R Positive		(n=1,745)	(n=369)		(n=290)	(n=1,824)	
Symptom Distress Index	High	7.0%	8.4%	0.402	9.0%	7.0%	0.271

--: Covariate not applicable for dependent variable.

Table F-5. Dependent Variable-Covariate Associations for the Gastrointestinal Assessment

Dependent Variable	Level	Age: Born ≥1942	Age: Born <1942	Age: p-Value	Race: Black	Race: Non-Black	Race: p-Value
Uncharacterized Hepatitis	Yes	(n=928) 2.3%	(n=1,179) 1.4%	0.215	(n=128) 2.3%	(n=1,979) 1.8%	0.896
Jaundice (Unspecified)	Yes	(n=914) 2.0%	(n=1,152) 2.5%	0.494	(n=127) 1.6%	(n=1,938) 2.3%	0.810
Chronic Liver Disease and Cirrhosis of the Liver (Alcohol-related)	Yes	(n=880) 4.2%	(n=1,118) 5.2%	0.358	(n=116) 9.5%	(n=1,882) 4.5%	0.025
Chronic Liver Disease and Cirrhosis of the Liver (Non-alcohol-related)	Yes	(n=933) 1.7%	(n=1,187) 1.0%	0.223	(n=128) 1.6%	(n=1,992) 1.3%	0.999
Liver Abscess and Sequelae of Chronic Liver Disease	Yes	(n=933) 0.0%	(n=1,188) 0.2%	0.588	(n=128) 0.0%	(n=1,993) 0.1%	0.999
Enlarged Liver (Hepatomegaly)	Yes	(n=932) 1.2%	(n=1,186) 2.5%	0.038	(n=127) 2.4%	(n=1,991) 1.9%	0.978
Other Liver Disorders	Yes	(n=927) 27.2%	(n=1,179) 26.2%	0.650	(n=128) 43.0%	(n=1,978) 25.6%	0.001
Current Hepatomegaly	Yes	(n=914) 0.5%	(n=1,177) 1.0%	0.343	(n=120) 0.0%	(n=1,971) 0.9%	0.618
AST		(n=913)	(n=1,177)		(n=120)	(n=1,970)	
(continuous)[a]		r=–0.025		0.247	$\bar{x}$=23.44	$\bar{x}$=22.90	0.454
(discrete)	High	7.8%	6.3%	0.214	6.7%	7.0%	0.999
ALT		(n=913)	(n=1,177)		(n=120)	(n=1,970)	
(continuous)[a]		r=–0.204		<0.001	$\bar{x}$=41.94	$\bar{x}$=42.54	0.596
(discrete)	High	10.0%	5.4%	0.001	7.5%	7.4%	0.999
GGT		(n=913)	(n=1,177)		(n=120)	(n=1,970)	
(continuous)[a]		r=–0.103		<0.001	$\bar{x}$=48.65	$\bar{x}$=42.70	0.012
(discrete)	High	12.6%	8.3%	0.002	13.3%	10.0%	0.309
Alkaline Phosphatase		(n=913)	(n=1,177)		(n=120)	(n=1,970)	
(continuous)[a]		r=0.003		0.909	$\bar{x}$=82.64	$\bar{x}$=80.40	0.274
(discrete)	High	2.5%	1.9%	0.435	3.3%	2.1%	0.582
Total Bilirubin		(n=913)	(n=1,177)		(n=120)	(n=1,970)	
(continuous)[a]		r=0.061		0.005	$\bar{x}$=0.489	$\bar{x}$=0.521	0.153
(discrete)	High	6.1%	5.6%	0.678	6.7%	5.8%	0.843
Direct Bilirubin	High	(n=913) 0.1%	(n=1,177) 0.4%	0.355	(n=120) 0.8%	(n=1,970) 0.3%	0.785

Table F-5. Dependent Variable-Covariate Associations for the Gastrointestinal Assessment (Continued)

Dependent Variable	Level	Age: Born ≥1942	Age: Born <1942	Age: p-Value	Race: Black	Race: Non-Black	Race: p-Value
Lactic Dehydrogenase		(n=913)	(n=1,175)		(n=119)	(n=1,969)	
(continuous)[a]		r=0.078		<0.001	$\bar{x}$=157.5	$\bar{x}$=153.7	0.131
(discrete)	High	9.9%	10.2%	0.846	12.6%	9.9%	0.427
Cholesterol		(n=913)	(n=1,177)		(n=120)	(n=1,970)	
(continuous)[b]		r=–0.049		0.025	$\bar{x}$=212.7	$\bar{x}$=211.5	0.726
(discrete)	High	16.2%	13.9%	0.166	12.5%	15.1%	0.524
HDL Cholesterol		(n=912)	(n=1,176)		(n=120)	(n=1,968)	
(continuous)[a]		r=0.035		0.114	$\bar{x}$=48.17	$\bar{x}$=44.70	0.002
(discrete)	Low	7.2%	8.1%	0.527	3.3%	8.0%	0.094
Cholesterol-HDL Ratio		(n=912)	(n=1,176)		(n=120)	(n=1,968)	
(continuous)[a]		r=–0.066		0.003	$\bar{x}$=4.39	$\bar{x}$=4.69	0.011
(discrete)	High	44.5%	38.7%	0.008	28.3%	42.0%	0.004
Triglycerides		(n=913)	(n=1,176)		(n=120)	(n=1,969)	
(continuous)[a]		r=–0.073		0.001	$\bar{x}$=93.0	$\bar{x}$=123.5	<0.001
(discrete)	High	24.0%	18.6%	0.003	6.7%	21.8%	0.001
Creatine Phosphokinase		(n=913)	(n=1,177)		(n=120)	(n=1,970)	
(continuous)[a]		r=–0.090		<0.001	$\bar{x}$=195.9	$\bar{x}$=102.0	<0.001
(discrete)	High	11.0%	7.4%	0.006	34.2%	7.1%	0.001
Serum Amylase		(n=913)	(n=1,177)		(n=120)	(n=1,970)	
(continuous)[a]		r=0.037		0.094	$\bar{x}$=72.71	$\bar{x}$=56.04	<0.001
(discrete)	High	2.7%	3.2%	0.602	10.8%	2.5%	0.001
Antibodies for Hepatitis A	Yes	(n=933) 23.5%	(n=1,187) 40.9%	0.001	(n=128) 43.8%	(n=1,992) 32.5%	0.012
Serological Evidence of Prior Hepatitis B Infection	Yes	(n=931) 11.2%	(n=1,187) 12.0%	0.579	(n=127) 26.8%	(n=1,991) 10.7%	0.001
Current Hepatitis B	Yes	(n=933) 0.2%	(n=1,188) 0.1%	0.834	(n=128) 1.6%	(n=1,993) 0.1%	0.001
Antibodies for Hepatitis C	Yes	(n=933) 1.8%	(n=1,188) 0.8%	0.071	(n=128) 4.7%	(n=1,993) 1.1%	0.002
Stool Hemoccult	Yes	(n=878) 2.6%	(n=1,152) 5.1%	0.006	(n=111) 5.4%	(n=1,919) 4.0%	0.614
Prealbumin		(n=913)	(n=1,177)		(n=120)	(n=1,970)	
(continuous)		r=–0.146		<0.001	$\bar{x}$=29.53	$\bar{x}$=29.59	0.901
(discrete)	Low	0.7%	1.5%	0.099	0.8%	1.2%	0.999

Table F-5. Dependent Variable-Covariate Associations for the Gastrointestinal Assessment (Continued)

Dependent Variable	Level	Age			Race		
		Born ≥1942	Born <1942	p-Value	Black	Non-Black	p-Value
Albumin		(n=913)	(n=1,177)		(n=120)	(n=1,970)	
(continuous)		r=–0.140		<0.001	$\bar{x}$=4,161.4	$\bar{x}$=4,201.2	0.209
(discrete)	Low	0.3%	0.8%	0.222	1.7%	0.6%	0.367
α-1-Acid Glycoprotein		(n=913)	(n=1,177)		(n=120)	(n=1,970)	
(continuous)[a]		r=–0.012		0.586	$\bar{x}$=81.87	$\bar{x}$=84.51	0.131
(discrete)	High	3.2%	4.1%	0.333	4.2%	3.7%	0.969
α-1-Antitrypsin		(n=913)	(n=1,177)		(n=120)	(n=1,970)	
(continuous)[b]		r=0.087		<0.001	$\bar{x}$=141.8	$\bar{x}$=148.3	0.006
(discrete)	Abn. Low	1.3%	1.4%	0.620	0.0%	1.5%	0.271
	Normal	98.2%	97.8%		100.0%	97.9%	
	Abn. High	0.4%	0.8%		0.0%	0.7%	
α-2-Macroglobulin		(n=913)	(n=1,177)		(n=120)	(n=1,970)	
(continuous)[a]		r=0.299		<0.001	$\bar{x}$=152.1	$\bar{x}$=172.2	<0.001
(discrete)	High	1.2%	5.1%	0.001	0.0%	3.6%	0.063
Apolipoprotein B		(n=913)	(n=1,177)		(n=120)	(n=1,970)	
(continuous)[b]		r=–0.050		0.023	$\bar{x}$=111.0	$\bar{x}$=111.1	0.951
(discrete)	High	53.6%	49.9%	0.103	50.0%	51.6%	0.810
C3 Complement		(n=913)	(n=1,177)		(n=120)	(n=1,970)	
(continuous)[a]		r=–0.048		0.027	$\bar{x}$=124.0	$\bar{x}$=118.4	0.002
(discrete)	Low	2.2%	2.0%	0.824	0.0%	2.2%	0.192
C4 Complement		(n=913)	(n=1,177)		(n=120)	(n=1,970)	
(continuous)[a]		r=–0.020		0.371	$\bar{x}$=29.00	$\bar{x}$=25.65	<0.001
(discrete)	Low	0.1%	0.3%	0.803	0.0%	0.2%	0.999
Haptoglobin		(n=913)	(n=1,177)		(n=120)	(n=1,970)	
(continuous)[b]		r=0.032		0.139	$\bar{x}$=119.8	$\bar{x}$=130.7	0.057
(discrete)	High	29.0%	30.5%	0.494	25.8%	30.1%	0.374
Transferrin		(n=913)	(n=1,177)		(n=120)	(n=1,970)	
(continuous)[a]		r=–0.050		0.022	$\bar{x}$=237.8	$\bar{x}$=251.7	<0.001
(discrete)	Low	8.2%	11.0%	0.043	20.8%	9.1%	0.001

Table F-5. Dependent Variable-Covariate Associations for the Gastrointestinal Assessment (Continued)

Dependent Variable	Level	Occupation: Officer	Occupation: Enlisted Flyer	Occupation: Enlisted Groundcrew	p-Value
Uncharacterized Hepatitis		(n=826)	(n=338)	(n=943)	
	Yes	1.5%	2.1%	2.0%	0.622
Jaundice (Unspecified)		(n=807)	(n=330)	(n=928)	
	Yes	3.1%	1.2%	1.9%	0.100
Chronic Liver Disease and Cirrhosis (Alcohol-related)		(n=798)	(n=318)	(n=882)	
	Yes	3.6%	6.0%	5.3%	0.142
Chronic Liver Disease and Cirrhosis (Non-alcohol-related)		(n=834)	(n=338)	(n=948)	
	Yes	1.0%	1.5%	1.6%	0.497
Liver Abscess and Sequelae of Chronic Liver Disease		(n=835)	(n=338)	(n=948)	
	Yes	0.1%	0.0%	0.1%	0.823
Enlarged Liver (Hepatomegaly)		(n=833)	(n=338)	(n=947)	
	Yes	1.7%	2.7%	1.9%	0.540
Other Liver Disorders		(n=824)	(n=338)	(n=944)	
	Yes	26.0%	26.0%	27.4%	0.756
Current Hepatomegaly		(n=830)	(n=335)	(n=926)	
	Yes	0.7%	0.6%	1.0%	0.753
AST		(n=830)	(n=335)	(n=925)	
(continuous)[a]		$\bar{x}$=23.37	$\bar{x}$=22.34	$\bar{x}$=22.76	0.073
(discrete)	High	6.7%	7.8%	6.8%	0.810
ALT		(n=830)	(n=335)	(n=925)	
(continuous)[a]		$\bar{x}$=41.96	$\bar{x}$=41.97	$\bar{x}$=43.19	0.069
(discrete)	High	5.4%	10.1%	8.2%	0.009
GGT		(n=830)	(n=335)	(n=925)	
(continuous)[a]		$\bar{x}$=41.38	$\bar{x}$=44.91	$\bar{x}$=43.87	0.026
(discrete)	High	8.2%	14.3%	10.5%	0.007
Alkaline Phosphatase		(n=830)	(n=335)	(n=925)	
(continuous)[a]		$\bar{x}$=77.43	$\bar{x}$=83.60	$\bar{x}$=82.29	<0.001
(discrete)	High	1.9%	3.0%	2.2%	0.535
Total Bilirubin		(n=830)	(n=335)	(n=925)	
(continuous)[a]		$\bar{x}$=0.544	$\bar{x}$=0.502	$\bar{x}$=0.504	0.001
(discrete)	High	6.9%	5.1%	5.2%	0.264
Direct Bilirubin		(n=830)	(n=335)	(n=925)	
	High	0.5%	0.0%	0.2%	0.328
Lactic Dehydrogenase		(n=829)	(n=334)	(n=925)	
(continuous)[a]		$\bar{x}$=154.2	$\bar{x}$=152.4	$\bar{x}$=154.2	0.531
(discrete)	High	10.3%	8.4%	10.5%	0.533

Table F-5. DependentbI'ariable-Covariate Associations for the Gastrointestinal Assessment.(Continued)

Dependent Variable	Level	Occupation: Officer	Occupation: Enlisted Flyer	Occupation: Enlisted Groundcrew	p-Value
Cholesterol		(n=830)	(n=335)	(n=925)	
(continuous)[b]		$\bar{x}$=208.5	$\bar{x}$=215.7	$\bar{x}$=212.9	0.004
(discrete)	High	12.9%	14.9%	16.8%	0.076
HDL Cholesterol		(n=829)	(n=334)	(n=925)	
(continuous)[a]		$\bar{x}$=46.67	$\bar{x}$=44.24	$\bar{x}$=43.59	<0.001
(discrete)	Low	5.2%	10.2%	9.1%	0.002
Cholesterol-HDL Ratio		(n=829)	(n=334)	(n=925)	
(continuous)[a]		$\bar{x}$=4.43	$\bar{x}$=4.84	$\bar{x}$=4.85	<0.001
(discrete)	High	32.6%	43.4%	48.2%	0.001
Triglycerides		(n=829)	(n=335)	(n=925)	
(continuous)[a]		$\bar{x}$=113.0	$\bar{x}$=131.3	$\bar{x}$=126.1	<0.001
(discrete)	High	17.1%	24.2%	23.2%	0.002
Creatine Phosphokinase		(n=830)	(n=335)	(n=925)	
(continuous)[a]		$\bar{x}$=104.9	$\bar{x}$=99.2	$\bar{x}$=109.2	0.038
(discrete)	High	8.4%	6.6%	10.3%	0.101
Serum Amylase		(n=830)	(n=335)	(n=925)	
(continuous)[a]		$\bar{x}$=56.62	$\bar{x}$=57.03	$\bar{x}$=57.06	0.906
(discrete)	High	3.5%	2.1%	2.9%	0.436
Antibodies for Hepatitis A		(n=834)	(n=338)	(n=948)	
	Yes	27.0%	47.3%	33.6%	0.001
Serological Evidence of Pri(		(n=834)	(n=338)	(n=946)	
Hepatitis B	Yes	6.0%	16.6%	14.9%	0.001
Current Hepatitis B		(n=835)	(n=338)	(n=948)	
	Yes	0.0%	0.0%	0.3%	0.156
Antibodies for Hepatitis C		(n=835)	(n=338)	(n=948)	
	Yes	0.6%	0.9%	2.0%	0.024
Stool Hemoccult		(n=815)	(n=325)	(n=890)	
	Yes	4.4%	2.8%	4.2%	0.431
Prealbumin		(n=830)	(n=335)	(n=925)	
(continuous)		$\bar{x}$=29.78	$\bar{x}$=29.44	$\bar{x}$=29.46	0.353
(discrete)	Low	1.4%	0.6%	1.1%	0.454
Albumin		(n=830)	(n=335)	(n=925)	
(continuous)		$\bar{x}$=4,191.6	$\bar{x}$=4,173.4	$\bar{x}$=4,214.6	0.115
(discrete)	Low	0.8%	0.3%	0.5%	0.516

Table F-5. Dependent Variable-Covariate Associations for the Gastrointestinal Assessment (Continued)

Dependent Variable	Level	Occupation: Officer	Occupation: Enlisted Flyer	Occupation: Enlisted Groundcrew	p-Value
α-1-Acid Glycoprotein		(n=830)	(n=335)	(n=925)	
(continuous)[a]		$\bar{x}$=81.68	$\bar{x}$=85.71	$\bar{x}$=86.34	<0.001
(discrete)	High	2.8%	4.8%	4.1%	0.170
α-1-Antitrypsin		(n=830)	(n=335)	(n=925)	
(continuous)[b]		$\bar{x}$=143.4	$\bar{x}$=153.0	$\bar{x}$=150.2	<0.001
(discrete)	Abnormal Low	2.3%	0.6%	0.9%	0.022
	Normal	97.5%	98.5%	98.3%	
	Abnormal High	0.2%	0.9%	0.9%	
α-2-Macroglobulin		(n=830)	(n=335)	(n=925)	
(continuous)[a]		$\bar{x}$=170.8	$\bar{x}$=177.2	$\bar{x}$=169.0	0.013
(discrete)	High	3.1%	4.8%	3.1%	0.315
Apolipoprotein B		(n=830)	(n=335)	(n=925)	
(continuous)[b]		$\bar{x}$=108.3	$\bar{x}$=114.3	$\bar{x}$=112.4	<0.001
(discrete)	High	47.1%	56.1%	53.7%	0.004
C3 Complement		(n=830)	(n=335)	(n=925)	
(continuous)[a]		$\bar{x}$=114.7	$\bar{x}$=120.5	$\bar{x}$=121.6	<0.001
(discrete)	Low	2.4%	1.8%	1.8%	0.654
C4 Complement		(n=830)	(n=335)	(n=925)	
(continuous)[a]		$\bar{x}$=25.21	$\bar{x}$=25.95	$\bar{x}$=26.35	<0.001
(discrete)	Low	0.4%	0.3%	0.0%	0.199
Haptoglobin		(n=830)	(n=335)	(n=925)	
(continuous)[b]		$\bar{x}$=118.7	$\bar{x}$=142.0	$\bar{x}$=136.3	<0.001
(discrete)	High	22.9%	36.1%	33.8%	0.001
Transferrin		(n=830)	(n=335)	(n=925)	
(continuous)[a]		$\bar{x}$=249.1	$\bar{x}$=252.8	$\bar{x}$=251.8	0.139
(discrete)	Low	9.2%	10.7%	9.9%	0.688

Dependent Variable	Level	Current Alcohol Use (drinks/day): 0–1	>1–4	>4	p-Value
Uncharacterized Hepatitis		--	--	--	--
Jaundice (Unspecified)		--	--	--	--
Chronic Liver Disease and Cirrhosis (Alcohol-related)		--	--	--	--
Chronic Liver Disease and Cirrhosis (Non-alcohol-related)		--	--	--	--

Table F-5. Dependent Variable-Covariate Associations for the Gastrointestinal Assessment (Continued)

Dependent Variable	Level	Current Alcohol Use (drinks/day) 0–1	>1–4	>4	p-Value
Liver Abscess and Sequelae of Chronic Liver Disease		--	--	--	--
Enlarged Liver (Hepatomegaly)		--	--	--	--
Other Liver Disorders		--	--	--	--
Current Hepatomegaly		(n=1,676)	(n=369)	(n=46)	
	Yes	0.7%	1.6%	0.0%	0.141
AST		(n=1,675)	(n=369)	(n=46)	
(continuous)[a]			r=0.114		<0.001
(discrete)	High	6.3%	8.1%	21.7%	0.001
ALT		(n=1,675)	(n=369)	(n=46)	
(continuous)[a]			r=0.057		0.009
(discrete)	High	7.3%	7.9%	8.7%	0.879
GGT		(n=1,675)	(n=369)	(n=46)	
(continuous)[a]			r=0.255		<0.001
(discrete)	High	7.3%	20.1%	34.8%	0.001
Total Bilirubin		(n=1,675)	(n=369)	(n=46)	
(continuous)[a]			r=0.093		<0.001
(discrete)	High	5.7%	5.4%	15.2%	0.023
Direct Bilirubin		(n=1,675)	(n=369)	(n=46)	
	High	0.1%	0.8%	2.2%	0.004
Lactic Dehydrogenase		(n=1,675)	(n=368)	(n=45)	
(continuous)[a]			r=–0.031		0.159
(discrete)	High	10.4%	9.0%	6.7%	0.533
Cholesterol		(n=1,675)	(n=369)	(n=46)	
(continuous)[b]			r=0.080		<0.001
(discrete)	High	13.7%	19.8%	19.6%	0.009
HDL Cholesterol		(n=1,673)	(n=369)	(n=46)	
(continuous)[a]			r=0.215		<0.001
(discrete)	Low	9.0%	2.4%	4.3%	0.001
Cholesterol-HDL Ratio		(n=1,673)	(n=369)	(n=46)	
(continuous)[a]			r=–0.152		<0.001
(discrete)	High	44.2%	29.3%	28.3%	0.001
Triglycerides		(n=1,675)	(n=368)	(n=46)	
(continuous)[a]			r=0.015		0.493
(discrete)	High	20.6%	21.7%	28.3%	0.417
Creatine Phosphokinase		(n=1,675)	(n=369)	(n=46)	
(continuous)[a]			r=–0.054		0.013
(discrete)	High	9.7%	5.1%	10.9%	0.018

Table F-5. Dependent Variable-Covariate Associations for the Gastrointestinal Assessment (Continued)

Dependent Variable	Level	Current Alcohol Use (drinks/day) 0–1	>1–4	>4	p-Value
Serum Amylase		(n=1,675)	(n=369)	(n=46)	
(continuous)[a]			r=–0.074		0.001
(discrete)	High	3.0%	3.3%	0.0%	0.471
Antibodies for Hepatitis A		(n=1,698)	(n=371)	(n=50)	
	Yes	33.5%	32.3%	30.0%	0.808
Serological Evidence of Prior Hepatitis B		(n=1,696)	(n=371)	(n=50)	
	Yes	12.0%	9.7%	14.0%	0.393
Current Hepatitis B		(n=1,699)	(n=371)	(n=50)	
	Yes	0.1%	0.0%	2.0%	0.002
Antibodies for Hepatitis C		(n=1,699)	(n=371)	(n=50)	
	Yes	1.2%	0.5%	6.0%	0.004
Stool Hemoccult		(n=1,633)	(n=355)	(n=42)	
	Yes	3.7%	5.4%	4.8%	0.364
Prealbumin		(n=1,675)	(n=369)	(n=46)	
(continuous)			r=0.117		<0.001
(discrete)	Low	0.8%	2.4%	4.3%	0.003
Albumin		(n=1,675)	(n=369)	(n=46)	
(continuous)			r=–0.015		0.506
(discrete)	Low	0.4%	1.4%	2.2%	0.047
α-1-Acid Glycoprotein		(n=1,675)	(n=369)	(n=46)	
(continuous)[a]			r=0.093		<0.001
(discrete)	High	3.0%	6.5%	6.5%	0.003
α-2-Macroglobulin		(n=1,675)	(n=369)	(n=46)	
(continuous)[a]			r=–0.047		0.031
(discrete)	High	3.7%	2.2%	2.2%	0.304
Apolipoprotein B		(n=1,675)	(n=369)	(n=46)	
(continuous)[b]			r=0.016		0.472
(discrete)	High	51.0%	53.1%	54.3%	0.714
C3 Complement		(n=1,675)	(n=369)	(n=46)	
(continuous)[a]			r=–0.132		<0.001
(discrete)	Low	1.6%	4.6%	0.0%	0.001
C4 Complement		(n=1,675)	(n=369)	(n=46)	
(continuous)[a]			r=–0.007		0.752
(discrete)	Low	0.1%	0.5%	0.0%	0.233
Haptoglobin		(n=1,675)	(n=369)	(n=46)	
(continuous)[b]			r=0.054		0.013
(discrete)	High	28.3%	35.5%	41.3%	0.005
Transferrin		(n=1,675)	(n=369)	(n=46)	
(continuous)[a]			r=0.050		0.022
(discrete)	Low	10.2%	8.7%	2.2%	0.143

Table F-5. Dependent Variable-Covariate Associations for the Gastrointestinal Assessment (Continued)

Dependent Variable	Level	Lifetime Alcohol History (drink-years) 0	>0-40	>40	p-Value
Uncharacterized Hepatitis		(n=117)	(n=1,370)	(n=612)	
	Yes	3.4%	2.3%	0.5%	0.010
Jaundice (Unspecified)		(n=115)	(n=1,339)	(n=603)	
	Yes	4.3%	2.3%	1.8%	0.250
Chronic Liver Disease and		--	(n=1,378)	(n=612)	
Cirrhosis (Alcohol-related)	Yes	--	1.3%	12.6%	0.001
Chronic Liver Disease and		(n=118)	(n=1,378)	(n=616)	
Cirrhosis (Non-alcohol-related)	Yes	1.7%	1.8%	0.2%	0.011
Liver Abscess and Sequelae of		(n=118)	(n=1,379)	(n=616)	
Chronic Liver Disease	Yes	0.0%	0.1%	0.2%	0.786
Enlarged Liver (Hepatomegaly)		(n=118)	(n=1,377)	(n=615)	
	Yes	0.8%	1.0%	4.2%	0.001
Other Liver Disorders		(n=117)	(n=1,368)	(n=613)	
	Yes	23.9%	25.1%	30.3%	0.043
Current Hepatomegaly		(n=118)	(n=1,363)	(n=603)	
	Yes	0.0%	0.7%	1.3%	0.190
AST		(n=118)	(n=1,362)	(n=603)	
(continuous)[a]			r=0.068		0.002
(discrete)	High	6.8%	6.1%	9.0%	0.071
ALT		(n=118)	(n=1,362)	(n=603)	
(continuous)[a]			r=–0.007		0.737
(discrete)	High	10.2%	7.3%	7.0%	0.474
GGT		(n=118)	(n=1,362)	(n=603)	
(continuous)[a]			r=0.096		<0.001
(discrete)	High	4.2%	8.7%	14.9%	0.001
Total Bilirubin		(n=118)	(n=1,362)	(n=603)	
(continuous)[a]			r=0.016		0.459
(discrete)	High	3.4%	5.7%	6.5%	0.415
Direct Bilirubin		(n=118)	(n=1,362)	(n=603)	
	High	0.0%	0.1%	0.8%	0.013
Lactic Dehydrogenase		(n=118)	(n=1,362)	(n=601)	
(continuous)[a]			r=0.001		0.952
(discrete)	High	14.4%	10.4%	8.3%	0.096
Cholesterol		(n=118)	(n=1,362)	(n=603)	
(continuous)[b]			r=0.035		0.108
(discrete)	High	11.9%	14.0%	17.9%	0.047
HDL Cholesterol		(n=118)	(n=1,360)	(n=603)	
(continuous)[a]			r=0.127		<0.001
(discrete)	Low	14.4%	8.4%	4.8%	0.001
Cholesterol-HDL Ratio		(n=118)	(n=1,360)	(n=603)	
(continuous)[a]			r=–0.098		<0.001
(discrete)	High	53.4%	43.3%	34.2%	0.001

Table F-5. Dependent Variable-Covariate Associations for the Gastrointestinal Assessment (Continued)

Dependent Variable	Level	Lifetime Alcohol History (drink-years) 0	>0-40	>40	p-Value
Triglycerides		(n=118)	(n=1,361)	(n=603)	
(continuous)[a]			r=–0.006		0.797
(discrete)	High	20.3%	21.0%	21.2%	0.976
Creatine Phosphokinase		(n=118)	(n=1,362)	(n=603)	
(continuous)[a]			r=–0.029		0.188
(discrete)	High	6.8%	9.7%	7.3%	0.163
Serum Amylase		(n=118)	(n=1,362)	(n=603)	
(continuous)[a]			r=–0.022		0.323
(discrete)	High	5.1%	2.8%	3.2%	0.369
Antibodies for Hepatitis A		(n=118)	(n=1,378)	(n=616)	
	Yes	45.8%	30.9%	35.9%	0.001
Serological Evidence of Prior		(n=118)	(n=1,376)	(n=616)	
Hepatitis B	Yes	5.9%	10.2%	16.1%	0.001
Current Hepatitis B		(n=118)	(n=1,379)	(n=616)	
	Yes	0.0%	0.1%	0.2%	0.911
Antibodies for Hepatitis C		(n=118)	(n=1,379)	(n=616)	
	Yes	0.0%	1.0%	1.9%	0.100
Stool Hemoccult		(n=107)	(n=1,331)	(n=585)	
	Yes	4.7%	3.6%	5.0%	0.364
Prealbumin		(n=118)	(n=1,362)	(n=603)	
(continuous)			r=0.030		0.170
(discrete)	Low	1.7%	0.6%	2.3%	0.003
Albumin		(n=118)	(n=1,362)	(n=603)	
(continuous)			r=–0.030		0.176
(discrete)	Low	0.8%	0.5%	0.8%	0.680
α-1-Acid Glycoprotein		(n=118)	(n=1,362)	(n=603)	
(continuous)[a]			r=0.094		<0.001
(discrete)	High	3.4%	3.1%	5.1%	0.082
α-1-Antitrypsin		(n=118)	(n=1,362)	(n=603)	
(continuous)[b]			r=0.077		0.001
(discrete)	Abn. Low	0.8%	1.3%	1.5%	0.259
	Normal	97.5%	98.3%	97.5%	
	Abn. High	1.7%	0.4%	1.0%	
α-2-Macroglobulin		(n=118)	(n=1,362)	(n=603)	
(continuous)[a]			r=0.015		0.501
(discrete)	High	9.3%	2.9%	3.3%	0.001
Apolipoprotein B		(n=118)	(n=1,362)	(n=603)	
(continuous)[b]			r=–0.002		0.919
(discrete)	High	50.8%	51.8%	50.9%	0.921
C3 Complement		(n=118)	(n=1,362)	(n=603)	
(continuous)[a]			r=–0.046		0.034
(discrete)	Low	0.0%	1.9%	2.8%	0.114

Table F-5. Dependent Variable-Covariate Associations for the Gastrointestinal Assessment (Continued)

Dependent Variable	Level	Lifetime Alcohol History (drink-years)			
		0	>0-40	>40	p-Value
C4 Complement		(n=118)	(n=1,362)	(n=603)	
(continuous)[a]			r=0.009		0.668
(discrete)	Low	0.0%	0.2%	0.2%	0.858
Haptoglobin		(n=118)	(n=1,362)	(n=603)	
(continuous)[b]			r=0.082		<0.001
(discrete)	High	30.5%	27.8%	34.2%	0.018
Transferrin		(n=118)	(n=1,362)	(n=603)	
(continuous)[a]			r=0.003		0.893
(discrete)	Low	11.9%	9.0%	11.1%	0.265

Dependent Variable	Level	Industrial Chemical Exposure			Degreasing Chemical Exposure		
		No	Yes	p-Value	No	Yes	p-Value
Uncharacterized Hepatitis	Yes	(n=797) 1.3%	(n=1,310) 2.1%	0.191	(n=748) 1.6%	(n=1,359) 1.9%	0.735
Jaundice (Unspecified)	Yes	(n=778) 2.7%	(n=1,287) 2.0%	0.395	(n=734) 2.0%	(n=1,331) 2.4%	0.710
Chronic Liver Disease and Cirrhosis of the Liver (Alcohol-related)	Yes	(n=756) 3.3%	(n=1,242) 5.6%	0.024	(n=711) 4.2%	(n=1,287) 5.1%	0.468
Chronic Liver Disease and Cirrhosis of the Liver (Non-alcohol-related)	Yes	(n=804) 1.1%	(n=1,316) 1.4%	0.661	(n=755) 1.2%	(n=1,365) 1.4%	0.851
Liver Abscess and Sequelae of Chronic Liver Disease	Yes	(n=804) 0.1%	(n=1,317) 0.1%	0.999	(n=755) 0.1%	(n=1,366) 0.1%	0.999
Enlarged Liver (Hepatomegaly)	Yes	(n=803) 1.9%	(n=1,315) 2.0%	0.988	(n=754) 1.9%	(n=1,364) 2.0%	0.975
Other Liver Disorders	Yes	(n=796) 26.0%	(n=1,310) 27.0%	0.644	(n=750) 25.5%	(n=1,356) 27.3%	0.394
Current Hepatomegaly	Yes	(n=799) 1.1%	(n=1,292) 0.6%	0.315	(n=749) 0.5%	(n=1,342) 1.0%	0.420
AST		(n=799)	(n=1,291)		(n=749)	(n=1,341)	
(continuous)[a]		$\bar{x}$=23.33	$\bar{x}$=22.69	0.063	$\bar{x}$=23.17	$\bar{x}$=22.80	0.294
(discrete)	High	7.1%	6.8%	0.850	7.2%	6.8%	0.783
ALT		(n=799)	(n=1,291)		(n=749)	(n=1,341)	
(continuous)[a]		$\bar{x}$=42.58	$\bar{x}$=42.45	0.805	$\bar{x}$=42.33	$\bar{x}$=42.60	0.619
(discrete)	High	7.8%	7.2%	0.700	7.1%	7.6%	0.721

Table F-5. Dependent Variable-Covariate Associations for the Gastrointestinal Assessment (Continued)

Dependent Variable	Level	Industrial Chemical Exposure			Degreasing Chemical Exposure		
		No	Yes	p-Value	No	Yes	p-Value
GGT		(n=799)	(n=1,291)		(n=749)	(n=1,341)	
(continuous)[a]		$\bar{x}$=43.27	$\bar{x}$=42.88	0.717	$\bar{x}$=42.55	$\bar{x}$=43.29	0.494
(discrete)	High	10.0%	10.3%	0.890	8.9%	10.9%	0.183
Alkaline Phosphatase		(n=799)	(n=1,291)		(n=749)	(n=1,341)	
(continuous)[a]		$\bar{x}$=79.87	$\bar{x}$=80.94	0.266	$\bar{x}$=79.91	$\bar{x}$=80.88	0.324
(discrete)	High	2.6%	1.9%	0.371	2.8%	1.9%	0.212
Total Bilirubin		(n=799)	(n=1,291)		(n=749)	(n=1,341)	
(continuous)[a]		$\bar{x}$=0.533	$\bar{x}$=0.511	0.052	$\bar{x}$=0.536	$\bar{x}$=0.510	0.020
(discrete)	High	5.6%	6.0%	0.827	5.6%	6.0%	0.812
Direct Bilirubin		(n=799)	(n=1,291)		(n=749)	(n=1,341)	
	High	0.4%	0.2%	0.862	0.3%	0.3%	0.999
Lactic Dehydrogenase		(n=797)	(n=1,291)		(n=747)	(n=1,341)	
(continuous)[a]		$\bar{x}$=153.8	$\bar{x}$=154.0	0.856	$\bar{x}$=153.9	$\bar{x}$=153.9	0.962
(discrete)	High	9.5%	10.4%	0.584	9.8%	10.2%	0.805
Cholesterol		(n=799)	(n=1,291)		(n=749)	(n=1,341)	
(continuous)[b]		$\bar{x}$=210.2	$\bar{x}$=212.4	0.193	$\bar{x}$=210.0	$\bar{x}$=212.5	0.157
(discrete)	High	14.0%	15.5%	0.392	13.5%	15.7%	0.187
HDL Cholesterol		(n=798)	(n=1,290)		(n=749)	(n=1,339)	
(continuous)[a]		$\bar{x}$=45.81	$\bar{x}$=44.33	0.005	$\bar{x}$=46.07	$\bar{x}$=44.25	0.001
(discrete)	Low	6.0%	8.8%	0.028	5.9%	8.7%	0.023
Cholesterol-HDL Ratio		(n=798)	(n=1,290)		(n=749)	(n=1,339)	
(continuous)[a]		$\bar{x}$=4.55	$\bar{x}$=4.75	<0.001	$\bar{x}$=4.52	$\bar{x}$=4.76	<0.001
(discrete)	High	35.7%	44.7%	0.001	36.2%	44.1%	0.001
Triglycerides		(n=799)	(n=1,290)		(n=749)	(n=1,340)	
(continuous)[a]		$\bar{x}$=116.4	$\bar{x}$=124.9	0.013	$\bar{x}$=114.7	$\bar{x}$=125.6	0.002
(discrete)	High	18.5%	22.5%	0.035	17.9%	22.7%	0.012
Creatine Phosphokinase		(n=799)	(n=1,291)		(n=749)	(n=1,341)	
(continuous)[a]		$\bar{x}$=104.8	$\bar{x}$=106.5	0.568	$\bar{x}$=107.7	$\bar{x}$=104.8	0.321
(discrete)	High	8.0%	9.5%	0.270	9.5%	8.7%	0.578
Serum Amylase		(n=799)	(n=1,291)		(n=749)	(n=1,341)	
(continuous)[a]		$\bar{x}$=56.47	$\bar{x}$=57.14	0.489	$\bar{x}$=56.75	$\bar{x}$=56.95	0.839
(discrete)	High	3.4%	2.8%	0.525	3.3%	2.8%	0.608
Antibodies for Hepatitis A		(n=804)	(n=1,316)		(n=755)	(n=1,365)	
	Yes	33.2%	33.2%	0.999	34.0%	32.7%	0.578

Table F-5. Dependent Variable-Covariate Associations for the Gastrointestinal Assessment (Continued)

Dependent Variable	Level	Industrial Chemical Exposure No	Industrial Chemical Exposure Yes	Industrial Chemical Exposure p-Value	Degreasing Chemical Exposure No	Degreasing Chemical Exposure Yes	Degreasing Chemical Exposure p-Value
Serological Evidence of Prior Hepatitis B Infection		(n=803)	(n=1,315)		(n=755)	(n=1,363)	
	Yes	10.1%	12.6%	0.090	10.6%	12.3%	0.286
Current Hepatitis B		(n=804)	(n=1,317)		(n=755)	(n=1,366)	
	Yes	0.1%	0.2%	0.999	0.1%	0.1%	0.999
Antibodies for Hepatitis C		(n=804)	(n=1,317)		(n=755)	(n=1,366)	
	Yes	0.5%	1.7%	0.022	0.7%	1.6%	0.096
Stool Hemoccult		(n=781)	(n=1,249)		(n=726)	(n=1,304)	
	Yes	5.4%	3.2%	0.021	4.8%	3.6%	0.224
Prealbumin		(n=799)	(n=1,291)		(n=749)	(n=1,341)	
(continuous)		$\bar{x}$=29.80	$\bar{x}$=29.45	0.130	$\bar{x}$=29.69	$\bar{x}$=29.52	0.452
(discrete)	High	1.3%	1.1%	0.891	1.1%	1.2%	0.966
Albumin		(n=799)	(n=1,291)		(n=749)	(n=1,341)	
(continuous)		$\bar{x}$=4,207.4	$\bar{x}$=4,193.6	0.364	$\bar{x}$=4,222.3	$\bar{x}$=4,185.8	0.017
(discrete)	High	0.8%	0.5%	0.761	0.5%	0.7%	0.927
α-1-Acid Glycoprotein		(n=799)	(n=1,291)		(n=749)	(n=1,341)	
(continuous)[a]		$\bar{x}$=83.38	$\bar{x}$=84.97	0.061	$\bar{x}$=83.46	$\bar{x}$=84.86	0.103
(discrete)	High	3.4%	3.9%	0.643	3.9%	3.6%	0.826
α-1-Antitrypsin		(n=799)	(n=1,291)		(n=749)	(n=1,341)	
(continuous)[b]		$\bar{x}$=145.7	$\bar{x}$=149.3	0.001	$\bar{x}$=146.2	$\bar{x}$=148.9	0.023
(discrete)	Abn. Low	2.1%	0.9%	0.037	1.6%	1.3%	0.805
	Normal	97.0%	98.6%		97.7%	98.1%	
	Abn. High	0.9%	0.5%		0.7%	0.6%	
α-2-Macroglobulin		(n=799)	(n=1,291)		(n=749)	(n=1,341)	
(continuous)[a]		$\bar{x}$=171.7	$\bar{x}$=170.6	0.560	$\bar{x}$=171.8	$\bar{x}$=170.6	0.529
(discrete)	High	2.6%	3.9%	0.161	3.2%	3.5%	0.812
Apolipoprotein B		(n=799)	(n=1,291)		(n=749)	(n=1,341)	
(continuous)[b]		$\bar{x}$=110.4	$\bar{x}$=111.5	0.319	$\bar{x}$=110.0	$\bar{x}$=111.7	0.131
(discrete)	High	50.8%	51.9%	0.662	49.3%	52.7%	0.141
C3 Complement		(n=799)	(n=1,291)		(n=749)	(n=1,341)	
(continuous)[a]		$\bar{x}$=116.7	$\bar{x}$=119.9	<0.001	$\bar{x}$=116.6	$\bar{x}$=119.9	<0.001
(discrete)	Low	1.9%	2.2%	0.766	2.4%	1.9%	0.502
C4 Complement		(n=799)	(n=1,291)		(n=749)	(n=1,341)	
(continuous)[a]		$\bar{x}$=25.51	$\bar{x}$=26.02	0.029	$\bar{x}$=25.63	$\bar{x}$=25.94	0.204
(discrete)	Low	0.4%	0.1%	0.317	0.5%	0.0%	0.031
Haptoglobin		(n=799)	(n=1,291)		(n=749)	(n=1,341)	
(continuous)[b]		$\bar{x}$=125.8	$\bar{x}$=132.7	0.013	$\bar{x}$=124.2	$\bar{x}$=133.4	0.001
(discrete)	High	26.5%	31.9%	0.010	25.8%	32.1%	0.003

Table F-5. Dependent Variable-Covariate Associations for the Gastrointestinal Assessment (Continued)

Dependent Variable	Level	Industrial Chemical Exposure			Degreasing Chemical Exposure		
		No	Yes	p-Value	No	Yes	p-Value
Transferrin		(n=799)	(n=1,291)		(n=749)	(n=1,341)	
(continuous)[a]		$\bar{x}$=250.3	$\bar{x}$=251.2	0.568	$\bar{x}$=248.2	$\bar{x}$=252.4	0.009
(discrete)	Low	8.8%	10.4%	0.256	9.5%	9.9%	0.805

Dependent Variable	Level	Current Wine Consumption (drinks of wine/day)			Lifetime Wine History (drink-years of wine)		
		0	>0	p-Value	0	>0	p-Value
Alkaline Phosphatase		(n=1,199)	(n=891)		(n=585)	(n=1,500)	
(continuous)[a]		r=–0.095		<0.001	r=–0.091		<0.001
(discrete)	High	2.6%	1.7%	0.215	2.2%	2.2%	0.999
α-1-Antitrypsin		(n=1,199)	(n=891)		--	--	--
(continuous)[b]		r=–0.077		<0.001	--		--
(discrete)	Abn. Low	1.0%	1.9%	0.031	--	--	--
	Normal	98.1%	97.9%		--	--	--
	Abn. High	0.9%	0.2%		--	--	--

[a] Analysis performed on natural logarithm scale; means transformed from natural logarithm scale.
[b] Analysis performed on square root scale; means transformed from square root scale.
--: Covariate or covariate category not applicable for dependent variable.

Note: Correlations (r) are based on total sample size and are not category-specific.

Table F-6. Dependent Variable-Covariate Associations for the Cardiovascular Assessment

Dependent Variable	Level	Age: Born ≥1942	Age: Born <1942	Age: p-Value	Race: Black	Race: Non-Black	Race: p-Value
Essential Hypertension		(n=919)	(n=1,151)		(n=123)	(n=1,947)	
	Yes	32.9%	48.0%	0.001	47.2%	40.9%	0.202
Heart Disease (Excluding Essential Hypertension)		(n=925)	(n=1,166)		(n=124)	(n=1,967)	
	Yes	52.3%	71.4%	0.001	69.4%	62.6%	0.156
Myocardial Infarction		(n=925)	(n=1,166)		(n=124)	(n=1,967)	
	Yes	3.7%	12.2%	0.001	5.6%	8.6%	0.327
Stroke or Transient Ischemia Attack		(n=925)	(n=1,166)		(n=124)	(n=1,967)	
	Yes	0.8%	1.5%	0.149	1.6%	1.2%	0.988
Systolic Blood Pressure (mm Hg)		(n=925)	(n=1,166)		(n=124)	(n=1,967)	
(continuous)[a]		r=0.214		<0.001	$\bar{x}$=126.7	$\bar{x}$=125.2	0.377
(discrete)	High	13.9%	26.9%	0.001	20.2%	21.3%	0.861
Diastolic Blood Pressure (mm Hg)		(n=925)	(n=1,166)		(n=124)	(n=1,967)	
(continuous)[b]		r=–0.057		0.009	$\bar{x}$=76.69	$\bar{x}$=74.46	0.010
(discrete)	High	5.3%	4.9%	0.747	8.9%	4.8%	0.075
Heart Sounds		(n=925)	(n=1,166)		(n=124)	(n=1,967)	
	Abnormal	2.4%	6.1%	0.001	4.8%	4.4%	0.999
Overall Electrocardiograph (ECG)		(n=925)	(n=1,166)		(n=124)	(n=1,967)	
	Abnormal	19.1%	40.7%	0.001	35.5%	30.9%	0.334
ECG: Right Bundle Branch Block		(n=925)	(n=1,166)		(n=124)	(n=1,967)	
	Yes	0.9%	3.9%	0.001	3.2%	2.5%	0.862
ECG: Left Bundle Branch Block		(n=925)	(n=1,166)		(n=124)	(n=1,967)	
	Yes	0.4%	1.1%	0.139	0.0%	0.9%	0.600
ECG: Non-specific ST- and T-Wave Changes		(n=925)	(n=1,166)		(n=124)	(n=1,967)	
	Yes	11.8%	23.4%	0.001	22.6%	18.0%	0.245
ECG: Bradycardia		(n=925)	(n=1,166)		(n=124)	(n=1,967)	
	Yes	3.1%	3.8%	0.503	1.6%	3.6%	0.356
ECG: Tachycardia		(n=925)	(n=1,166)		(n=124)	(n=1,967)	
	Yes	0.3%	0.6%	0.555	0.8%	0.5%	0.999
ECG: Arrhythmia		(n=925)	(n=1,166)		(n=124)	(n=1,967)	
	Yes	2.4%	8.3%	0.001	5.6%	5.7%	0.999
ECG: Evidence of Prior Myocardial Infarction		(n=925)	(n=1,166)		(n=124)	(n=1,967)	
	Yes	1.8%	6.0%	0.001	1.6%	4.3%	0.218
ECG: Other Diagnoses		(n=925)	(n=1,166)		(n=124)	(n=1,967)	
	Yes	0.2%	0.2%	0.999	0.8%	0.2%	0.578

Table F-6. Dependent Variable-Covariate Associations for the Cardiovascular Assessment (Continued)

Dependent Variable	Level	Age: Born ≥1942	Age: Born <1942	Age: p-Value	Race: Black	Race: Non-Black	Race: p-Value
Funduscopic Examination	Abnormal	(n=925) 6.4%	(n=1,164) 17.4%	0.001	(n=124) 16.1%	(n=1,965) 12.3%	0.262
Carotid Bruits	Present	(n=925) 1.1%	(n=1,166) 3.9%	0.001	(n=124) 3.2%	(n=1,967) 2.6%	0.918
Radial Pulses	Abnormal	(n=925) 0.5%	(n=1,166) 0.5%	0.999	(n=124) 2.4%	(n=1,967) 0.4%	0.018
Femoral Pulses	Abnormal	(n=925) 0.8%	(n=1,165) 2.3%	0.009	(n=124) 3.2%	(n=1,966) 1.5%	0.278
Popliteal Pulses	Abnormal	(n=925) 1.1%	(n=1,164) 3.5%	0.001	(n=124) 4.0%	(n=1,965) 2.3%	0.377
Dorsalis Pedis Pulses	Abnormal	(n=925) 4.4%	(n=1,164) 10.6%	0.001	(n=124) 11.3%	(n=1,965) 7.6%	0.195
Posterior Tibial Pulses	Abnormal	(n=925) 3.0%	(n=1,162) 8.1%	0.001	(n=124) 6.5%	(n=1,963) 5.8%	0.921
Leg Pulses	Abnormal	(n=925) 5.6%	(n=1,162) 14.2%	0.001	(n=124) 14.5%	(n=1,963) 10.1%	0.162
Peripheral Pulses	Abnormal	(n=925) 5.8%	(n=1,162) 14.5%	0.001	(n=124) 16.1%	(n=1,963) 10.3%	0.061
Intermittent Claudication and Vascular Insufficiency (ICVI) Index	Abnormal	(n=924) 3.0%	(n=1,166) 4.3%	0.164	(n=124) 3.2%	(n=1,966) 3.8%	0.950

Dependent Variable	Level	Occupation: Officer	Occupation: Enlisted Flyer	Occupation: Enlisted Groundcrew	p-Value
Essential Hypertension	Yes	(n=809) 40.4%	(n=333) 45.3%	(n=928) 40.5%	0.254
Heart Disease (Excluding Essential Hypertension)	Yes	(n=818) 68.7%	(n=335) 66.6%	(n=938) 56.7%	0.001
Myocardial Infarction	Yes	(n=818) 8.6%	(n=335) 9.3%	(n=938) 8.0%	0.763
Stroke or Transient Ischemia Attack	Yes	(n=818) 1.2%	(n=335) 0.9%	(n=938) 1.3%	0.854
Systolic Blood Pressure (mm Hg)		(n=818)	(n=335)	(n=938)	
(continuous)[a]		$\bar{x}$=126.1	$\bar{x}$=127.1	$\bar{x}$=123.9	0.005
(discrete)	High	23.2%	23.6%	18.6%	0.029
Diastolic Blood Pressure (mm Hg)		(n=818)	(n=335)	(n=938)	
(continuous)[b]		$\bar{x}$=74.19	$\bar{x}$=75.16	$\bar{x}$=74.74	0.224
(discrete)	High	5.1%	4.8%	5.1%	0.965

Table F-6. Dependent Variable-Covariate Associations for the Cardiovascular Assessment (Continued)

		Occupation			
Dependent Variable	Level	Officer	Enlisted Flyer	Enlisted Groundcrew	p-Value
Heart Sounds		(n=818)	(n=335)	(n=938)	
	Abnormal	4.5%	5.4%	4.1%	0.597
Overall Electrocardiograph (ECG)		(n=818)	(n=335)	(n=938)	
	Abnormal	34.6%	36.4%	26.3%	0.001
ECG: Right Bundle Branch Block		(n=818)	(n=335)	(n=938)	
	Yes	2.6%	4.5%	1.9%	0.040
ECG: Left Bundle Branch Block		(n=818)	(n=335)	(n=938)	
	Yes	1.0%	0.3%	0.9%	0.498
ECG: Non-specific ST- and T-Wave Changes		(n=818)	(n=335)	(n=938)	
	Yes	20.2%	20.0%	16.0%	0.052
ECG: Bradycardia		(n=818)	(n=335)	(n=938)	
	Yes	5.6%	3.0%	1.8%	0.001
ECG: Tachycardia		(n=818)	(n=335)	(n=938)	
	Yes	0.2%	0.9%	0.5%	0.329
ECG: Arrhythmia		(n=818)	(n=335)	(n=938)	
	Yes	6.1%	7.5%	4.7%	0.137
ECG: Evidence of Prior Myocardial Infarction		(n=818)	(n=335)	(n=938)	
	Yes	4.6%	4.8%	3.5%	0.412
ECG: Other Diagnoses		(n=818)	(n=335)	(n=938)	
	Yes	0.1%	0.0%	0.3%	0.436
Funduscopic Examination		(n=817)	(n=334)	(n=938)	
	Abnormal	11.1%	18.6%	11.5%	0.001
Carotid Bruits		(n=818)	(n=335)	(n=938)	
	Present	2.2%	3.9%	2.7%	0.276
Radial Pulses		(n=818)	(n=335)	(n=938)	
	Abnormal	0.5%	0.0%	0.7%	0.264
Femoral Pulses		(n=818)	(n=334)	(n=938)	
	Abnormal	1.8%	2.4%	1.2%	0.265
Popliteal Pulses		(n=817)	(n=334)	(n=938)	
	Abnormal	2.3%	2.7%	2.5%	0.934
Dorsalis Pedis Pulses		(n=817)	(n=334)	(n=938)	
	Abnormal	7.2%	10.5%	7.5%	0.147
Posterior Tibial Pulses		(n=817)	(n=332)	(n=938)	
	Abnormal	5.5%	8.1%	5.3%	0.151
Leg Pulses		(n=817)	(n=332)	(n=938)	
	Abnormal	9.3%	14.2%	10.0%	0.044
Peripheral Pulses		(n=817)	(n=332)	(n=938)	
	Abnormal	9.7%	14.2%	10.3%	0.075
ICVI Index		(n=818)	(n=335)	(n=937)	
	Abnormal	3.4%	5.7%	3.3%	0.123

Table F-6. Dependent Variable-Covariate Associations for the Cardiovascular Assessment (Continued)

Dependent Variable	Level	Lifetime Alcohol History (drink-years) 0	>0-40	>40	p-Value
Essential Hypertension		(n=118)	(n=1,348)	(n=596)	
	Yes	39.0%	38.5%	48.2%	0.001
Heart Disease (Excluding Essential Hypertension)		(n=118)	(n=1,360)	(n=605)	
	Yes	62.7%	63.0%	63.1%	0.996
Myocardial Infarction		(n=118)	(n=1,360)	(n=605)	
	Yes	10.2%	7.9%	9.4%	0.410
Stroke or Transient Ischemia Attack		(n=118)	(n=1,360)	(n=605)	
	Yes	1.7%	1.0%	1.7%	0.373
Systolic Blood Pressure (mm Hg)		(n=118)	(n=1,360)	(n=605)	
(continuous)[a]			r=0.086		<0.001
(discrete)	High	19.5%	19.9%	24.6%	0.051
Diastolic Blood Pressure (mm Hg)		(n=118)	(n=1,360)	(n=605)	
(continuous)[b]			r=0.034		0.126
(discrete)	High	3.4%	4.8%	6.1%	0.317
Heart Sounds		(n=118)	(n=1,360)	(n=605)	
	Abnormal	4.2%	4.0%	5.5%	0.374
Overall Electrocardiograph (ECG)		(n=118)	(n=1,360)	(n=605)	
	Abnormal	39.0%	29.9%	32.6%	0.082
ECG: Right Bundle Branch Block		(n=118)	(n=1,360)	(n=605)	
	Yes	1.7%	2.7%	2.5%	0.781
ECG: Left Bundle Branch Block		(n=118)	(n=1,360)	(n=605)	
	Yes	0.8%	1.0%	0.5%	0.578
ECG: Non-specific ST- and T-Wave Changes		(n=118)	(n=1,360)	(n=605)	
	Yes	26.3%	18.5%	15.9%	0.024
ECG: Bradycardia		(n=118)	(n=1,360)	(n=605)	
	Yes	0.8%	3.2%	4.6%	0.072
ECG: Tachycardia		(n=118)	(n=1,360)	(n=605)	
	Yes	1.7%	0.2%	0.8%	0.029
ECG: Arrhythmia		(n=118)	(n=1,360)	(n=605)	
	Yes	9.3%	6.0%	4.5%	0.093
ECG: Evidence of Prior Myocardial Infarction		(n=118)	(n=1,360)	(n=605)	
	Yes	5.1%	4.3%	3.8%	0.786
ECG: Other Diagnoses		(n=118)	(n=1,360)	(n=605)	
	Yes	0.0%	0.2%	0.2%	0.857
Funduscopic Examination		(n=118)	(n=1,359)	(n=604)	
	Abnormal	14.4%	11.2%	14.9%	0.057
Carotid Bruits		(n=118)	(n=1,360)	(n=605)	
	Present	2.5%	2.3%	3.6%	0.228
Radial Pulses		(n=118)	(n=1,360)	(n=605)	
	Abnormal	0.0%	0.2%	1.3%	0.006

Table F-6. Dependent Variable-Covariate Associations for the Cardiovascular Assessment (Continued)

Dependent Variable	Level	Lifetime Alcohol History (drink-years) 0	>0–40	>40	p-Value
Femoral Pulses		(n=118)	(n=1,359)	(n=605)	
	Abnormal	0.0%	1.1%	3.1%	0.002
Popliteal Pulses		(n=118)	(n=1,358)	(n=605)	
	Abnormal	0.8%	1.9%	4.0%	0.013
Dorsalis Pedis Pulses		(n=118)	(n=1,358)	(n=605)	
	Abnormal	8.5%	6.6%	10.6%	0.009
Posterior Tibial Pulses		(n=118)	(n=1,356)	(n=605)	
	Abnormal	3.4%	5.2%	7.9%	0.027
Leg Pulses		(n=118)	(n=1,356)	(n=605)	
	Abnormal	11.0%	9.0%	13.4%	0.013
Peripheral Pulses		(n=118)	(n=1,356)	(n=605)	
	Abnormal	11.0%	9.1%	14.0%	0.005
ICVI Index		(n=118)	(n=1,360)	(n=605)	
	Abnormal	1.7%	3.5%	4.6%	0.239

Dependent Variable	Level	Current Alcohol Use (drinks/day) 0–1	>1–4	>4	p-Value
Essential Hypertension		--	--	--	--
Heart Disease (Excluding Essential Hypertension)		--	--	--	--
Myocardial Infarction		--	--	--	--
Stroke or Transient Ischemia Attack		--	--	--	--
Systolic Blood Pressure (mm Hg)		(n=1,673)	(n=367)	(n=50)	
(continuous)[a]			r=0.008		0.715
(discrete)	High	20.8%	24.0%	14.0%	0.182
Diastolic Blood Pressure (mm Hg)		(n=1,673)	(n=367)	(n=50)	
(continuous)[b]			r=0.025		0.253
(discrete)	High	4.8%	5.7%	8.0%	0.497
Heart Sounds		(n=1,673)	(n=367)	(n=50)	
	Abnormal	4.7%	3.5%	4.0%	0.634
Overall Electrocardiograph (ECG)		(n=1,673)	(n=367)	(n=50)	
	Abnormal	30.6%	34.6%	26.0%	0.236
ECG: Right Bundle Branch Block		(n=1,673)	(n=367)	(n=50)	
	Yes	2.7%	2.2%	2.0%	0.827
ECG: Left Bundle Branch Block		(n=1,673)	(n=367)	(n=50)	
	Yes	0.8%	0.8%	2.0%	0.638
ECG: Non-specific ST- and T-Wave Changes		(n=1,673)	(n=367)	(n=50)	
	Yes	18.7%	17.4%	10.0%	0.263

Table F-6. Dependent Variable-Covariate Associations for the Cardiovascular Assessment (Continued)

Dependent Variable	Level	Current Alcohol Use (drinks/day) 0–1	>1–4	>4	p-Value
ECG: Bradycardia		(n=1,673)	(n=367)	(n=50)	
	Yes	3.2%	5.2%	2.0%	0.139
ECG: Tachycardia		(n=1,673)	(n=367)	(n=50)	
	Yes	0.5%	0.5%	0.0%	0.872
ECG: Arrhythmia		(n=1,673)	(n=367)	(n=50)	
	Yes	5.5%	6.8%	4.0%	0.538
ECG: Evidence of Prior		(n=1,673)	(n=367)	(n=50)	
Myocardial Infarction	Yes	4.4%	3.3%	4.0%	0.636
ECG: Other Diagnoses		(n=1,673)	(n=367)	(n=50)	
	Yes	0.2%	0.3%	0.0%	0.889
Funduscopic Examination		(n=1,671)	(n=367)	(n=50)	
	Abnormal	12.6%	11.7%	14.0%	0.846
Carotid Bruits		(n=1,673)	(n=367)	(n=50)	
	Present	2.6%	3.3%	0.0%	0.390
Radial Pulses		(n=1,673)	(n=367)	(n=50)	
	Abnormal	0.3%	1.6%	0.0%	0.005
Femoral Pulses		(n=1,672)	(n=367)	(n=50)	
	Abnormal	1.0%	4.4%	4.0%	0.001
Popliteal Pulses		(n=1,672)	(n=366)	(n=50)	
	Abnormal	1.9%	4.9%	4.0%	0.002
Dorsalis Pedis Pulses		(n=1,672)	(n=366)	(n=50)	
	Abnormal	7.3%	10.1%	10.0%	0.165
Posterior Tibial Pulses		(n=1,670)	(n=366)	(n=50)	
	Abnormal	5.0%	9.3%	10.0%	0.003
Leg Pulses		(n=1,670)	(n=366)	(n=50)	
	Abnormal	9.6%	13.4%	14.0%	0.073
Peripheral Pulses		(n=1,670)	(n=366)	(n=50)	
	Abnormal	9.8%	14.2%	14.0%	0.036
ICVI Index		(n=1,673)	(n=367)	(n=50)	
	Abnormal	3.5%	4.1%	8.0%	0.239

Dependent Variable	Level	Lifetime Cigarette Smoking History (pack-years) 0	>0–10	>10	p-Value
Essential Hypertension		(n=582)	(n=543)	(n=942)	
	Yes	38.0%	43.1%	42.3%	0.155
Heart Disease (Excluding Essential		(n=587)	(n=550)	(n=951)	
Hypertension)	Yes	61.2%	62.9%	64.2%	0.474
Myocardial Infarction		(n=587)	(n=550)	(n=951)	
	Yes	4.9%	5.6%	12.2%	0.001
Stroke or Transient Ischemia Attack		(n=587)	(n=550)	(n=951)	
	Yes	0.9%	1.1%	1.4%	0.647

Table F-6. Dependent Variable-Covariate Associations for the Cardiovascular Assessment (Continued)

Dependent Variable	Level	Lifetime Cigarette Smoking History (pack-years) 0	>0–10	>10	p-Value
Systolic Blood Pressure (mm Hg)		(n=587)	(n=550)	(n=951)	
(continuous)[a]			r=0.044		0.045
(discrete)	High	19.9%	20.0%	22.6%	0.338
Diastolic Blood Pressure (mm Hg)		(n=587)	(n=550)	(n=951)	
(continuous)[b]			r=–0.066		0.003
(discrete)	High	4.1%	7.8%	4.1%	0.003
Heart Sounds		(n=587)	(n=550)	(n=951)	
	Abnormal	2.9%	4.5%	5.4%	0.074
Overall Electrocardiograph (ECG)		(n=587)	(n=550)	(n=951)	
	Abnormal	28.3%	27.6%	35.0%	0.002
ECG: Right Bundle Branch Block		(n=587)	(n=550)	(n=951)	
	Yes	2.2%	1.5%	3.5%	0.048
ECG: Left Bundle Branch Block		(n=587)	(n=550)	(n=951)	
	Yes	0.5%	1.1%	0.8%	0.549
ECG: Non-specific ST- and T-Wave Changes		(n=587)	(n=550)	(n=951)	
	Yes	17.9%	15.6%	20.0%	0.107
ECG: Bradycardia		(n=587)	(n=550)	(n=951)	
	Yes	4.3%	4.0%	2.7%	0.216
ECG: Tachycardia		(n=587)	(n=550)	(n=951)	
	Yes	0.5%	0.5%	0.4%	0.936
ECG: Arrhythmia		(n=587)	(n=550)	(n=951)	
	Yes	4.1%	5.5%	6.7%	0.091
ECG: Evidence of Prior Myocardial Infarction		(n=587)	(n=550)	(n=951)	
	Yes	2.9%	2.7%	5.8%	0.003
ECG: Other Diagnoses		(n=587)	(n=550)	(n=951)	
	Yes	0.2%	0.4%	0.1%	0.539
Funduscopic Examination		(n=587)	(n=550)	(n=949)	
	Abnormal	8.9%	11.6%	15.2%	0.001
Carotid Bruits		(n=587)	(n=550)	(n=951)	
	Present	1.0%	2.4%	3.9%	0.003
Radial Pulses		(n=587)	(n=550)	(n=951)	
	Abnormal	0.2%	0.5%	0.7%	0.329
Femoral Pulses		(n=587)	(n=550)	(n=950)	
	Abnormal	0.3%	1.3%	2.6%	0.002
Popliteal Pulses		(n=587)	(n=549)	(n=950)	
	Abnormal	0.5%	2.0%	3.9%	0.001
Dorsalis Pedis Pulses		(n=587)	(n=549)	(n=950)	
	Abnormal	2.9%	6.2%	11.9%	0.001
Posterior Tibial Pulses		(n=587)	(n=549)	(n=948)	
	Abnormal	3.1%	3.6%	8.8%	0.001

Table F-6. Dependent Variable-Covariate Associations for the Cardiovascular Assessment (Continued)

Dependent Variable	Level	Lifetime Cigarette Smoking History (pack-years) 0	>0–10	>10	p-Value
Leg Pulses		(n=587)	(n=549)	(n=948)	
	Abnormal	5.1%	7.5%	15.3%	0.001
Peripheral Pulses		(n=587)	(n=549)	(n=948)	
	Abnormal	5.3%	7.7%	15.7%	0.001
ICVI Index		(n=587)	(n=550)	(n=951)	
	Abnormal	1.4%	2.5%	5.9%	0.001

Dependent Variable	Level	Current Cigarette Smoking (cigarettes/day) 0-Never	0-Former	>0–20	>20	p-Value
Essential Hypertension		--	--	--	--	--
Heart Disease (Excluding Essential Hypertension)		--	--	--	--	--
Myocardial Infarction		--	--	--	--	--
Stroke or Transient Ischemia Attack		--	--	--	--	--
Systolic Blood Pressure (mm Hg)		(n=587)	(n=1,101)	(n=266)	(n=136)	
(continuous)[a]			r=–0.064			0.004
(discrete)	High	19.9%	22.7%	20.3%	16.2%	0.236
Diastolic Blood Pressure (mm Hg)		(n=587)	(n=1,101)	(n=266)	(n=136)	
(continuous)[b]			r=–0.076			0.001
(discrete)	High	4.1%	5.7%	5.3%	3.7%	0.438
Heart Sounds		(n=587)	(n=1,101)	(n=266)	(n=136)	
	Abnormal	2.9%	5.7%	3.4%	2.9%	0.030
Overall Electrocardiograph (ECG)		(n=587)	(n=1,101)	(n=266)	(n=136)	
	Abnormal	28.3%	32.8%	35.0%	23.5%	0.028
ECG: Right Bundle Branch Block		(n=587)	(n=1,101)	(n=266)	(n=136)	
	Yes	2.2%	2.9%	2.3%	2.2%	0.810
ECG: Left Bundle Branch Block		(n=587)	(n=1,101)	(n=266)	(n=136)	
	Yes	0.5%	1.2%	0.0%	0.7%	0.195
ECG: Non-specific ST- and T-Wave Changes		(n=587)	(n=1,101)	(n=266)	(n=136)	
	Yes	17.9%	19.2%	19.2%	11.0%	0.135
ECG: Bradycardia		(n=587)	(n=1,101)	(n=266)	(n=136)	
	Yes	4.3%	3.1%	4.1%	2.2%	0.466
ECG: Tachycardia		(n=587)	(n=1,101)	(n=266)	(n=136)	
	Yes	0.5%	0.5%	0.4%	0.7%	0.965
ECG: Arrhythmia		(n=587)	(n=1,101)	(n=266)	(n=136)	
	Yes	4.1%	6.8%	5.3%	4.4%	0.117
ECG: Evidence of Prior Myocardial Infarction		(n=587)	(n=1,101)	(n=266)	(n=136)	
	Yes	2.9%	4.7%	4.5%	4.4%	0.344

Table F-6. Dependent Variable-Covariate Associations for the Cardiovascular Assessment (Continued)

Dependent Variable	Level	Current Cigarette Smoking (cigarettes/day)				
		0-Never	0-Former	>0–20	>20	p-Value
ECG: Other Diagnoses		(n=587)	(n=1,101)	(n=266)	(n=136)	
	Yes	0.2%	0.2%	0.0%	0.7%	0.451
Funduscopic Examination		(n=587)	(n=1,100)	(n=266)	(n=135)	
	Abnormal	8.9%	14.0%	13.5%	14.1%	0.019
Carotid Bruits		(n=587)	(n=1,101)	(n=266)	(n=136)	
	Present	1.0%	3.1%	4.1%	3.7%	0.023
Radial Pulses		(n=587)	(n=1,101)	(n=266)	(n=136)	
	Abnormal	0.2%	0.4%	1.9%	0.7%	0.010
Femoral Pulses		(n=587)	(n=1,100)	(n=266)	(n=136)	
	Abnormal	0.3%	1.2%	4.9%	4.4%	0.001
Popliteal Pulses		(n=587)	(n=1,099)	(n=266)	(n=136)	
	Abnormal	0.5%	2.0%	7.1%	5.1%	0.001
Dorsalis Pedis Pulses		(n=587)	(n=1,099)	(n=266)	(n=136)	
	Abnormal	2.9%	8.0%	13.9%	16.2%	0.001
Posterior Tibial Pulses		(n=587)	(n=1,098)	(n=265)	(n=136)	
	Abnormal	3.1%	5.6%	10.6%	11.0%	0.001
Leg Pulses		(n=587)	(n=1,098)	(n=265)	(n=136)	
	Abnormal	5.1%	10.7%	16.2%	19.9%	0.001
Peripheral Pulses		(n=587)	(n=1,098)	(n=265)	(n=136)	
	Abnormal	5.3%	10.8%	17.4%	19.9%	0.001
ICVI Index		(n=587)	(n=1,101)	(n=266)	(n=136)	
	Abnormal	1.4%	3.5%	7.9%	8.1%	0.001

Dependent Variable	Level	Cholesterol (mg/dl)			
		≤200	>200-239	>239	p-Value
Essential Hypertension		(n=785)	(n=838)	(n=447)	
	Yes	41.0%	42.7%	38.9%	0.415
Heart Disease (Excluding Essential Hypertension)	Yes	(n=794) 66.6%	(n=848) 63.3%	(n=449) 55.9%	0.001
Myocardial Infarction		(n=794)	(n=848)	(n=449)	
	Yes	11.5%	8.0%	3.8%	0.001
Stroke or Transient Ischemia Attack		(n=794)	(n=848)	(n=449)	
	Yes	1.4%	1.3%	0.7%	0.503
Systolic Blood Pressure (mm Hg)		(n=794)	(n=848)	(n=449)	
(continuous)[a]			r=0.055		0.012
(discrete)	High	18.1%	22.6%	23.8%	0.025
Diastolic Blood Pressure (mm Hg)		(n=794)	(n=848)	(n=449)	
(continuous)[b]			r=0.096		<0.001
(discrete)	High	4.0%	5.3%	6.5%	0.159
Heart Sounds		(n=794)	(n=848)	(n=449)	
	Abnormal	4.2%	4.5%	4.9%	0.828

Table F-6. Dependent Variable-Covariate Associations for the Cardiovascular Assessment (Continued)

Dependent Variable	Level	Cholesterol (mg/dl) ≤200	>200-239	>239	p-Value
Overall Electrocardiograph (ECG)		(n=794)	(n=848)	(n=449)	
	Abnormal	34.4%	29.7%	28.3%	0.041
ECG: Right Bundle Branch Block		(n=794)	(n=848)	(n=449)	
	Yes	3.0%	2.1%	2.7%	0.512
ECG: Left Bundle Branch Block		(n=794)	(n=848)	(n=449)	
	Yes	0.9%	0.7%	0.9%	0.906
ECG: Non-specific ST- and T-Wave Changes		(n=794)	(n=848)	(n=449)	
	Yes	19.8%	17.0%	18.0%	0.339
ECG: Bradycardia		(n=794)	(n=848)	(n=449)	
	Yes	4.0%	3.5%	2.4%	0.344
ECG: Tachycardia		(n=794)	(n=848)	(n=449)	
	Yes	0.3%	0.6%	0.7%	0.493
ECG: Arrhythmia		(n=794)	(n=848)	(n=449)	
	Yes	6.4%	5.3%	5.1%	0.523
ECG: Evidence of Prior Myocardial Infarction		(n=794)	(n=848)	(n=449)	
	Yes	5.8%	3.7%	2.2%	0.007
ECG: Other Diagnoses		(n=794)	(n=848)	(n=449)	
	Yes	0.4%	0.0%	0.2%	0.213
Funduscopic Examination		(n=792)	(n=848)	(n=449)	
	Abnormal	13.1%	11.4%	13.4%	0.480
Carotid Bruits		(n=794)	(n=848)	(n=449)	
	Present	2.6%	2.7%	2.7%	0.996
Radial Pulses		(n=794)	(n=848)	(n=449)	
	Abnormal	0.5%	0.6%	0.4%	0.938
Femoral Pulses		(n=793)	(n=848)	(n=449)	
	Abnormal	1.5%	1.7%	1.8%	0.935
Popliteal Pulses		(n=793)	(n=847)	(n=449)	
	Abnormal	2.1%	2.6%	2.7%	0.786
Dorsalis Pedis Pulses		(n=793)	(n=847)	(n=449)	
	Abnormal	7.2%	8.3%	8.2%	0.678
Posterior Tibial Pulses		(n=793)	(n=845)	(n=449)	
	Abnormal	4.9%	6.9%	5.6%	0.235
Leg Pulses		(n=793)	(n=845)	(n=449)	
	Abnormal	9.0%	11.4%	11.1%	0.237
Peripheral Pulses		(n=793)	(n=845)	(n=449)	
	Abnormal	9.2%	11.7%	11.4%	0.226
ICVI Index		(n=793)	(n=848)	(n=449)	
	Abnormal	3.8%	3.5%	4.0%	0.909

Table F-6. Dependent Variable-Covariate Associations for the Cardiovascular Assessment (Continued)

Dependent Variable	Level	HDL Cholesterol (mg/dl) 0-35	HDL Cholesterol (mg/dl) >35	p-Value	Cholesterol-HDL Ratio 0-5	Cholesterol-HDL Ratio >5	p-Value
Essential Hypertension		(n=369)	(n=1,700)		(n=1,217)	(n=852)	
	Yes	45.0%	40.5%	0.124	38.7%	45.0%	0.005
Heart Disease (Excluding Essential Hypertension)		(n=372)	(n=1,718)		(n=1,230)	(n=860)	
	Yes	61.3%	63.4%	0.484	64.6%	60.7%	0.074
Myocardial Infarction		(n=372)	(n=1,718)		(n=1,230)	(n=860)	
	Yes	11.8%	7.7%	0.012	8.1%	8.8%	0.622
Stroke or Transient Ischemia Attack		(n=372)	(n=1,718)		(n=1,230)	(n=860)	
	Yes	1.3%	1.2%	0.979	1.2%	1.2%	0.999
Systolic Blood Pressure		(n=372)	(n=1,718)		(n=1,230)	(n=860)	
(mm Hg) (continuous)[a]		r=–0.025		0.245	r=0.062		0.005
(discrete)	High	21.5%	21.1%	0.928	19.5%	23.6%	0.028
Diastolic Blood Pressure (mm Hg)		(n=372)	(n=1,718)		(n=1,230)	(n=860)	
(continuous)[b]		r=–0.008		0.707	r=0.063		0.004
(discrete)	High	5.4%	5.0%	0.869	4.7%	5.6%	0.432
Heart Sounds		(n=372)	(n=1,718)		(n=1,230)	(n=860)	
	Abnormal	5.6%	4.2%	0.274	4.2%	4.8%	0.630
Overall Electrocardiograph (ECG)		(n=372)	(n=1,718)		(n=1,230)	(n=860)	
	Abnormal	33.6%	30.7%	0.297	31.9%	30.2%	0.455
ECG: Right Bundle Branch Block		(n=372)	(n=1,718)		(n=1,230)	(n=860)	
	Yes	3.2%	2.4%	0.496	2.7%	2.4%	0.840
ECG: Left Bundle Branch Block		(n=372)	(n=1,718)		(n=1,230)	(n=860)	
	Yes	1.3%	0.7%	0.348	0.9%	0.7%	0.806
ECG: Non-specific ST- and T-Wave Changes		(n=372)	(n=1,718)		(n=1,230)	(n=860)	
	Yes	21.5%	17.6%	0.089	17.8%	19.0%	0.541
ECG: Bradycardia		(n=372)	(n=1,718)		(n=1,230)	(n=860)	
	Yes	1.6%	3.9%	0.043	4.5%	2.1%	0.005
ECG: Tachycardia		(n=372)	(n=1,718)		(n=1,230)	(n=860)	
	Yes	0.5%	0.5%	0.999	0.3%	0.7%	0.372
ECG: Arrhythmia		(n=372)	(n=1,718)		(n=1,230)	(n=860)	
	Yes	4.3%	6.0%	0.248	6.3%	4.9%	0.215
ECG: Evidence of Prior Myocardial Infarction		(n=372)	(n=1,718)		(n=1,230)	(n=860)	
	Yes	5.4%	3.9%	0.250	4.2%	4.1%	0.947
ECG: Other Diagnoses		(n=372)	(n=1,718)		(n=1,230)	(n=860)	
	Yes	0.0%	0.2%	0.782	0.2%	0.1%	0.882
Funduscopic Examination		(n=372)	(n=1,716)		(n=1,228)	(n=860)	
	Abnormal	11.3%	12.8%	0.489	13.4%	11.2%	0.139
Carotid Bruits		(n=372)	(n=1,718)		(n=1,230)	(n=860)	
	Present	1.9%	2.9%	0.382	2.5%	2.9%	0.688

Table F-6. Dependent Variable-Covariate Associations for the Cardiovascular Assessment (Continued)

		HDL Cholesterol (mg/dl)			Cholesterol-HDL Ratio		
Dependent Variable	**Level**	**0-35**	**>35**	**p-Value**	**0-5**	**>5**	**p-Value**
Radial Pulses		(n=372)	(n=1,718)		(n=1,230)	(n=860)	
	Abnormal	0.5%	0.5%	0.999	0.5%	0.6%	0.999
Femoral Pulses		(n=371)	(n=1,718)		(n=1,230)	(n=859)	
	Abnormal	1.6%	1.6%	0.999	1.5%	1.7%	0.855
Popliteal Pulses		(n=371)	(n=1,717)		(n=1,229)	(n=859)	
	Abnormal	2.4%	2.4%	0.999	2.1%	2.9%	0.311
Dorsalis Pedis Pulses		(n=371)	(n=1,717)		(n=1,229)	(n=859)	
	Abnormal	8.6%	7.7%	0.615	7.1%	9.0%	0.135
Posterior Tibial Pulses		(n=371)	(n=1,715)		(n=1,229)	(n=857)	
	Abnormal	5.1%	6.0%	0.592	5.8%	6.0%	0.943
Leg Pulses		(n=371)	(n=1,715)		(n=1,229)	(n=857)	
	Abnormal	10.5%	10.4%	0.999	9.8%	11.3%	0.284
Peripheral Pulses		(n=371)	(n=1,715)		(n=1,229)	(n=857)	
	Abnormal	10.5%	10.7%	0.976	10.1%	11.6%	0.321
ICVI Index		(n=372)	(n=1,717)		(n=1,229)	(n=860)	
	Abnormal	5.1%	3.4%	0.164	3.6%	4.0%	0.745

		Body Fat			Personality Type		
Dependent Variable	**Level**	**Lean/Normal**	**Obese**	**p-Value**	**Type A**	**Type B**	**p-Value**
Essential Hypertension	Yes	(n=1,472) 35.2%	(n=598) 56.2%	0.001	(n=803) 38.4%	(n=1,264) 43.0%	0.039
Heart Disease (Excluding Essential Hypertension)	Yes	(n=1,482) 62.7%	(n=609) 63.7%	0.696	(n=812) 62.8%	(n=1,276) 63.0%	0.963
Myocardial Infarction		(n=1,482)	(n=609)		(n=812)	(n=1,276)	
	Yes	8.6%	8.0%	0.760	8.9%	8.1%	0.577
Stroke or Transient Ischemia Attack	Yes	(n=1,482) 1.1%	(n=609) 1.3%	0.923	(n=812) 0.9%	(n=1,276) 1.4%	0.359
Systolic Blood Pressure (mm Hg)		(n=1,482)	(n=609)		(n=812)	(n=1,276)	
(continuous)[a]		r=0.185		<0.001	$\bar{x}$=124.4	$\bar{x}$=125.9	0.061
(discrete)	High	18.6%	27.4%	0.001	19.2%	22.5%	0.083
Diastolic Blood Pressure (mm Hg)		(n=1,482)	(n=609)		(n=812)	(n=1,276)	
(continuous)[b]		r=0.122		<0.001	$\bar{x}$=74.40	$\bar{x}$=74.71	0.457
(discrete)	High	4.5%	6.6%	0.058	4.3%	5.5%	0.273
Heart Sounds		(n=1,482)	(n=609)		(n=812)	(n=1,276)	
	Abnormal	4.1%	5.3%	0.303	4.1%	4.7%	0.562
Overall Electrocardiograph (ECG)	Abnormal	(n=1,482) 29.4%	(n=609) 35.5%	0.008	(n=812) 27.8%	(n=1,276) 33.2%	0.011

Table F-6. Dependent Variable-Covariate Associations for the Cardiovascular Assessment (Continued)

Dependent Variable	Level	Body Fat			Personality Type		
		Lean/Normal	Obese	p-Value	Type A	Type B	p-Value
ECG: Right Bundle Branch Block	Yes	(n=1,482) 2.4%	(n=609) 3.0%	0.591	(n=812) 2.6%	(n=1,276) 2.6%	0.999
ECG: Left Bundle Branch Block	Yes	(n=1,482) 0.7%	(n=609) 1.0%	0.769	(n=812) 0.9%	(n=1,276) 0.8%	0.999
ECG: Non-specific ST- and T-Wave Changes	Yes	(n=1,482) 16.3%	(n=609) 23.0%	0.001	(n=812) 16.9%	(n=1,276) 19.2%	0.199
ECG: Bradycardia	Yes	(n=1,482) 4.5%	(n=609) 1.0%	0.001	(n=812) 3.8%	(n=1,276) 3.3%	0.606
ECG: Tachycardia	Yes	(n=1,482) 0.3%	(n=609) 0.8%	0.268	(n=812) 0.2%	(n=1,276) 0.6%	0.366
ECG: Arrhythmia	Yes	(n=1,482) 5.6%	(n=609) 5.9%	0.861	(n=812) 5.7%	(n=1,276) 5.6%	0.999
ECG: Evidence of Prior Myocardial Infarction	Yes	(n=1,482) 3.8%	(n=609) 5.1%	0.213	(n=812) 3.7%	(n=1,276) 4.5%	0.454
ECG: Other Diagnoses	Yes	(n=1,482) 0.3%	(n=609) 0.0%	0.464	(n=812) 0.2%	(n=1,276) 0.2%	0.999
Funduscopic Examination	Abnormal	(n=1,481) 11.1%	(n=608) 15.8%	0.004	(n=811) 9.2%	(n=1,275) 14.4%	0.001
Carotid Bruits	Present	(n=1,482) 2.8%	(n=609) 2.3%	0.589	(n=812) 2.3%	(n=1,276) 2.8%	0.596
Radial Pulses	Abnormal	(n=1,482) 0.6%	(n=609) 0.3%	0.640	(n=812) 0.6%	(n=1,276) 0.5%	0.890
Femoral Pulses	Abnormal	(n=1,481) 1.6%	(n=609) 1.6%	0.999	(n=811) 1.0%	(n=1,276) 1.9%	0.150
Popliteal Pulses	Abnormal	(n=1,480) 2.5%	(n=609) 2.3%	0.909	(n=810) 1.6%	(n=1,276) 2.8%	0.101
Dorsalis Pedis Pulses	Abnormal	(n=1,480) 8.2%	(n=609) 6.9%	0.342	(n=810) 6.4%	(n=1,276) 8.6%	0.081
Posterior Tibial Pulses	Abnormal	(n=1,478) 6.5%	(n=609) 4.3%	0.062	(n=809) 4.2%	(n=1,275) 6.7%	0.020
Leg Pulses	Abnormal	(n=1,478) 11.2%	(n=609) 8.4%	0.062	(n=809) 8.2%	(n=1,275) 11.7%	0.012
Peripheral Pulses	Abnormal	(n=1,478) 11.6%	(n=609) 8.4%	0.034	(n=809) 8.7%	(n=1,275) 11.8%	0.026
ICVI Index	Abnormal	(n=1,481) 3.6%	(n=609) 3.9%	0.845	(n=811) 4.2%	(n=1,276) 3.4%	0.394

Table F-6. Dependent Variable-Covariate Associations for the Cardiovascular Assessment (Continued)

Dependent Variable	Level	Family History of Heart Disease			Family History of Heart Disease Before Age 45		
		Yes	No	p-Value	Yes	No	p-Value
Essential Hypertension	Yes	(n=1,246) 45.3%	(n=808) 35.3%	0.001	(n=243) 50.2%	(n=1,784) 40.1%	0.003
Heart Disease (Excluding Essential Hypertension)	Yes	(n=1,262) 66.6%	(n=813) 57.4%	0.001	(n=249) 69.9%	(n=1,798) 62.0%	0.018
Myocardial Infarction	Yes	(n=1,262) 9.4%	(n=813) 6.9%	0.058	(n=249) 10.8%	(n=1,798) 8.0%	0.154
Stroke or Transient Ischemia Attack	Yes	(n=1,262) 1.2%	(n=813) 1.2%	0.999	(n=249) 1.2%	(n=1,798) 1.2%	0.999
Systolic Blood Pressure (mm Hg)		(n=1,262)	(n=813)		(n=249)	(n=1,798)	
(continuous)[a]		$\bar{x}$ =125.8	$\bar{x}$ =124.6	0.130	$\bar{x}$ =125.2	$\bar{x}$ =125.3	0.938
(discrete)	High	23.3%	18.3%	0.008	20.1%	21.2%	0.734
Diastolic Blood Pressure (mm Hg)		(n=1,262)	(n=813)		(n=249)	(n=1,798)	
(continuous)[b]		$\bar{x}$ =74.71	$\bar{x}$ =74.47	0.557	$\bar{x}$ =74.06	$\bar{x}$ =74.60	0.384
(discrete)	High	5.3%	4.7%	0.588	4.4%	4.9%	0.835
Heart Sounds	Abnormal	(n=1,262) 4.9%	(n=813) 3.7%	0.226	(n=249) 6.4%	(n=1,798) 4.1%	0.133
Overall Electrocardiograph (ECG)	Abnormal	(n=1,262) 35.3%	(n=813) 24.6%	0.001	(n=249) 36.1%	(n=1,798) 30.4%	0.076
ECG: Right Bundle Branch Block	Yes	(n=1,262) 3.2%	(n=813) 1.7%	0.060	(n=249) 2.8%	(n=1,798) 2.6%	0.999
ECG: Left Bundle Branch Block	Yes	(n=1,262) 0.6%	(n=813) 1.1%	0.251	(n=249) 0.4%	(n=1,798) 0.8%	0.732
ECG: Non-specific ST- and T-Wave Changes	Yes	(n=1,262) 21.1%	(n=813) 14.0%	0.001	(n=249) 22.5%	(n=1,798) 17.6%	0.076
ECG: Bradycardia	Yes	(n=1,262) 3.4%	(n=813) 3.7%	0.826	(n=249) 2.4%	(n=1,798) 3.6%	0.430
ECG: Tachycardia	Yes	(n=1,262) 0.7%	(n=813) 0.1%	0.116	(n=249) 0.8%	(n=1,798) 0.4%	0.783
ECG: Arrhythmia	Yes	(n=1,262) 6.4%	(n=813) 4.6%	0.090	(n=249) 7.2%	(n=1,798) 5.3%	0.284
ECG: Evidence of Prior Myocardial Infarction	Yes	(n=1,262) 4.4%	(n=813) 3.7%	0.525	(n=249) 4.4%	(n=1,798) 4.0%	0.890
ECG: Other Diagnoses	Yes	(n=1,262) 0.1%	(n=813) 0.4%	0.339	(n=249) 0.0%	(n=1,798) 0.2%	0.999

Table F-6. Dependent Variable-Covariate Associations for the Cardiovascular Assessment (Continued)

		Family History of Heart Disease			Family History of Heart Disease Before Age 45		
Dependent Variable	**Level**	**Yes**	**No**	**p-Value**	**Yes**	**No**	**p-Value**
Funduscopic Examination		(n=1,262)	(n=811)		(n=249)	(n=1,796)	
	Abnormal	12.8%	12.1%	0.700	14.5%	12.2%	0.376
Carotid Bruits		(n=1,262)	(n=813)		(n=249)	(n=1,798)	
	Present	2.9%	2.5%	0.689	3.6%	2.6%	0.484
Radial Pulses		(n=1,262)	(n=813)		(n=249)	(n=1,798)	
	Abnormal	0.6%	0.5%	0.999	0.8%	0.5%	0.881
Femoral Pulses		(n=1,261)	(n=813)		(n=249)	(n=1,797)	
	Abnormal	1.8%	1.4%	0.517	1.2%	1.7%	0.736
Popliteal Pulses		(n=1,260)	(n=813)		(n=249)	(n=1,796)	
	Abnormal	2.6%	2.2%	0.663	2.8%	2.4%	0.900
Dorsalis Pedis Pulses		(n=1,260)	(n=813)		(n=249)	(n=1,796)	
	Abnormal	8.1%	7.6%	0.762	8.4%	7.9%	0.846
Posterior Tibial Pulses		(n=1,258)	(n=813)		(n=248)	(n=1,795)	
	Abnormal	6.0%	5.7%	0.790	6.0%	5.8%	0.987
Leg Pulses		(n=1,258)	(n=813)		(n=248)	(n=1,795)	
	Abnormal	10.6%	10.3%	0.920	9.7%	10.5%	0.784
Peripheral Pulses		(n=1,258)	(n=813)		(n=248)	(n=1,795)	
	Abnormal	10.8%	10.7%	0.995	10.1%	10.8%	0.833
ICVI Index		(n=1,262)	(n=813)		(n=249)	(n=1,798)	
	Abnormal	4.0%	3.2%	0.433	2.8%	3.8%	0.533

Table F-6. Dependent Variable-Covariate Associations for the Cardiovascular Assessment (Continued)

Dependent Variable	Level	Diabetic Class: Normal	Diabetic Class: Impaired	Diabetic Class: Diabetic	Diabetic Class: p-Value	Blood Pressure Medication: Yes	Blood Pressure Medication: No	Blood Pressure Medication: p-Value
Essential Hypertension	Yes	(n=1,429) 34.6%	(n=271) 52.4%	(n=345) 59.4%	0.001	--	--	--
Heart Disease (Excluding Essential Hypertension)	Yes	(n=1,441) 60.8%	(n=273) 64.1%	(n=351) 69.5%	0.009	--	--	--
Myocardial Infarction	Yes	(n=1,441) 6.8%	(n=273) 9.9%	(n=351) 14.2%	0.001	--	--	--
Stroke or Transient Ischemia Attack	Yes	(n=1,441) 1.0%	(n=273) 1.1%	(n=351) 1.4%	0.828	--	--	--
Systolic Blood Pressure (mm Hg)		(n=1,441)	(n=273)	(n=351)		(n=617)	(n=1,474)	
(continuous)[a]		$\bar{x}$ =123.0	$\bar{x}$ =129.3	$\bar{x}$ =131.8	<0.001	$\bar{x}$ =128.6	$\bar{x}$ =123.9	<0.001
(discrete)	High	17.1%	28.6%	31.9%	0.001	27.6%	18.5%	0.001
Diastolic Blood Pressure (mm Hg)		(n=1,441)	(n=273)	(n=351)		(n=617)	(n=1,474)	
(continuous)[b]		$\bar{x}$ =74.32	$\bar{x}$ =75.94	$\bar{x}$ =74.41	0.030	$\bar{x}$ =74.86	$\bar{x}$ =74.48	0.392
(discrete)	High	4.5%	7.3%	5.4%	0.140	7.3%	4.1%	0.004
Heart Sounds	Abnormal	(n=1,441) 3.7%	(n=273) 5.5%	(n=351) 6.0%	0.113	--	--	--
Overall Electrocardiograph (ECG)	Abnormal	(n=1,441) 26.4%	(n=273) 37.0%	(n=351) 46.7%	0.001	--	--	--
ECG: Right Bundle Branch Block	Yes	(n=1,441) 1.9%	(n=273) 2.6%	(n=351) 5.4%	0.001	--	--	--
ECG: Left Bundle Branch Block	Yes	(n=1,441) 0.7%	(n=273) 1.1%	(n=351) 1.1%	0.613	--	--	--
ECG: Non-specific ST- and T-Wave Changes	Yes	(n=1,441) 14.6%	(n=273) 24.5%	(n=351) 29.3%	0.001	--	--	--
ECG: Bradycardia	Yes	(n=1,441) 4.5%	(n=273) 0.4%	(n=351) 1.7%	0.001	--	--	--
ECG: Tachycardia	Yes	(n=1,441) 0.2%	(n=273) 0.4%	(n=351) 1.4%	0.008	--	--	--
ECG: Arrhythmia	Yes	(n=1,441) 5.2%	(n=273) 5.1%	(n=351) 8.0%	0.121	--	--	--
ECG: Evidence of Prior Myocardial Infarction	Yes	(n=1,441) 2.8%	(n=273) 5.1%	(n=351) 9.4%	0.001	--	--	--
ECG: Other Diagnoses	Yes	(n=1,441) 0.3%	(n=273) 0.0%	(n=351) 0.0%	0.420	--	--	--

Table F-6. Dependent Variable-Covariate Associations for the Cardiovascular Assessment (Continued)

Dependent Variable	Level	Diabetic Class				Blood Pressure Medication		
		Normal	Impaired	Diabetic	p-Value	Yes	No	p-Value
Funduscopic Examination		(n=1,440)	(n=273)	(n=350)				
	Abnormal	10.3%	14.3%	20.0%	0.001	--	--	--
Carotid Bruits		(n=1,441)	(n=273)	(n=351)				
	Present	2.1%	2.9%	5.1%	0.007	--	--	--
Radial Pulses		(n=1,441)	(n=273)	(n=351)				
	Abnormal	0.3%	0.4%	1.1%	0.152	--	--	--
Femoral Pulses		(n=1,440)	(n=273)	(n=351)				
	Abnormal	1.2%	1.1%	3.7%	0.003	--	--	--
Popliteal Pulses		(n=1,439)	(n=273)	(n=351)				
	Abnormal	1.7%	1.8%	6.0%	0.001	--	--	--
Dorsalis Pedis Pulses		(n=1,439)	(n=273)	(n=351)				
	Abnormal	6.7%	5.5%	14.0%	0.001	--	--	--
Posterior Tibial Pulses		(n=1,437)	(n=273)	(n=351)				
	Abnormal	4.1%	5.5%	13.4%	0.001	--	--	--
Leg Pulses		(n=1,437)	(n=273)	(n=351)				
	Abnormal	8.7%	8.4%	18.8%	0.001	--	--	--
Peripheral Pulses		(n=1,437)	(n=273)	(n=351)				
	Abnormal	8.9%	8.4%	19.4%	0.001	--	--	--
ICVI Index		(n=1,440)	(n=273)	(n=351)				
	Abnormal	2.6%	2.9%	9.1%	0.001	--	--	--

[a] Analysis performed on natural logarithm scale; means transformed from natural logarithm scale.
[b] Analysis performed on square root scale; means transformed from square root scale.
--: Covariate not applicable for dependent variable.

Note: Correlations (r) are based on total sample size and are not category-specific.

Table F-7. Dependent Variable-Covariate Associations for the Hematology Assessment

Dependent Variable	Level	Age			Race		
		Born ≥1942	Born <1942	p-Value	Black	Non-Black	p-Value
RBC Count (million/mm³)		(n=928)	(n=1,187)		(n=128)	(n=1,987)	
(continuous)		r=–0.181		<0.001	$\bar{x}$=4.99	$\bar{x}$=4.95	0.291
(discrete)	Abn. Low	2.1%	7.0%	0.001	7.8%	4.6%	0.001
	Normal	97.2%	91.8%		86.7%	94.7%	
	Abn. High	0.7%	1.2%		5.5%	0.7%	
WBC Count (thousand/mm³)		(n=928)	(n=1,187)		(n=128)	(n=1,987)	
(continuous)[a]		r=–0.010		0.658	$\bar{x}$=5.94	$\bar{x}$=6.71	<0.001
(discrete)	Abn. Low	5.9%	4.9%	0.456	18.8%	4.5%	0.001
	Normal	90.2%	91.7%		78.9%	91.8%	
	Abn. High	3.9%	3.4%		2.3%	3.7%	
Hemoglobin (gm/dl)		(n=928)	(n=1,187)		(n=128)	(n=1,987)	
(continuous)		r=–0.137		<0.001	$\bar{x}$=14.77	$\bar{x}$=15.36	<0.001
(discrete)	Abn. Low	4.5%	8.3%	0.002	17.2%	6.0%	0.001
	Normal	95.0%	91.3%		82.8%	93.5%	
	Abn. High	0.5%	0.4%		0.0%	0.5%	
Hematocrit (percent)		(n=928)	(n=1,187)		(n=128)	(n=1,987)	
(continuous)		r=–0.121		<0.001	$\bar{x}$=44.49	$\bar{x}$=45.65	<0.001
(discrete)	Abn. Low	1.3%	3.2%	0.014	4.7%	2.2%	0.169
	Normal	98.5%	96.5%		95.3%	97.5%	
	Abn. High	0.2%	0.3%		0.0%	0.3%	
Platelet Count (thousand/mm³)		(n=926)	(n=1,179)		(n=127)	(n=1,978)	
(continuous)[b]		r=–0.120		<0.001	$\bar{x}$=203.7	$\bar{x}$=205.3	0.723
(discrete)	Abn. Low	1.9%	3.7%	0.022	1.6%	3.0%	0.526
	Normal	97.9%	95.7%		97.6%	96.6%	
	Abn. High	0.2%	0.6%		0.8%	0.4%	
Prothrombin Time (seconds)		(n=793)	(n=911)		(n=110)	(n=1,594)	
(continuous)[a]		r=0.096		<0.001	$\bar{x}$=10.49	$\bar{x}$=10.49	0.947
(discrete)	High	0.8%	1.9%	0.077	2.7%	1.3%	0.386
RBC Morphology		(n=928)	(n=1,187)		(n=128)	(n=1,987)	
	Abnormal	5.2%	8.0%	0.013	14.1%	6.3%	0.001

Table F-7. Dependent Variable-Covariate Associations for the Hematology Assessment (Continued)

Dependent Variable	Level	Age: Born ≥1942	Age: Born <1942	Age: p-Value	Race: Black	Race: Non-Black	Race: p-Value
Absolute Neutrophils (segs)		(n=2,115)			(n=128)	(n=1,987)	
(thousand/mm³)[a]		r=0.006		0.767	$\bar{x}$=3.13	$\bar{x}$=3.88	<0.001
Absolute Neutrophils (bands) (thousand/mm³)		(n=1,757)			(n=97)	(n=1,660)	
(continuous)[a]	Nonzero	r=0.071		0.003	$\bar{x}$=0.120	$\bar{x}$=0.200	<0.001
(discrete)		(n=928)	(n=1,187)		(n=128)	(n=1,987)	
	Zero	17.1%	16.8%	0.868	24.2%	16.5%	0.032
Absolute Lymphocytes		(n=2,115)			(n=128)	(n=1,987)	
(thousand/mm³)[a]		r=–0.116		<0.001	$\bar{x}$=1.87	$\bar{x}$=1.75	0.035
Absolute Monocytes		(n=2,115)			(n=128)	(n=1,987)	
(thousand/mm³)[b]		r=0.044		0.043	$\bar{x}$=0.466	$\bar{x}$=0.480	0.455
Absolute Eosinophils (thousand/mm³)		(n=1,856)			(n=109)	(n=1,747)	
(continuous)[a]	Nonzero	r=0.026		0.256	$\bar{x}$=0.145	$\bar{x}$=0.161	0.132
(discrete)		(n=928)	(n=1,187)		(n=128)	(n=1,987)	
	Zero	12.8%	11.8%	0.516	14.8%	12.1%	0.432
Absolute Basophils (thousand/mm³)		(n=953)			(n=54)	(n=899)	
(continuous)[a]	Nonzero	r=0.017		0.610	$\bar{x}$=0.068	$\bar{x}$=0.080	0.006
(discrete)		(n=928)	(n=1,187)		(n=128)	(n=1,987)	
	Zero	56.9%	53.4%	0.120	57.8%	54.8%	0.561

Table F-7. Dependent Variable-Covariate Associations for the Hematology Assessment (Continued)

Dependent Variable	Level	Occupation: Officer	Occupation: Enlisted Flyer	Occupation: Enlisted Groundcrew	p-Value
RBC Count (million/mm^3)		(n=834)	(n=338)	(n=943)	
(continuous)		$\bar{x}$=4.90	$\bar{x}$=4.95	$\bar{x}$=5.01	<0.001
(discrete)	Abnormal Low	5.6%	5.3%	3.9%	0.502
	Normal	93.6%	93.5%	95.1%	
	Abnormal High	0.8%	1.2%	1.0%	
WBC Count (thousand/mm^3)		(n=834)	(n=338)	(n=943)	
(continuous)[a]		$\bar{x}$=6.33	$\bar{x}$=6.80	$\bar{x}$=6.91	<0.001
(discrete)	Abnormal Low	6.1%	4.7%	4.9%	0.056
	Normal	91.6%	90.0%	91.0%	
	Abnormal High	2.3%	5.3%	4.1%	
Hemoglobin (gm/dl)		(n=834)	(n=338)	(n=943)	
(continuous)		$\bar{x}$=15.26	$\bar{x}$=15.34	$\bar{x}$=15.37	0.076
(discrete)	Abnormal Low	6.5%	8.6%	6.2%	0.609
	Normal	93.0%	91.1%	93.3%	
	Abnormal High	0.5%	0.3%	0.5%	
Hematocrit (percent)		(n=834)	(n=338)	(n=943)	
(continuous)		$\bar{x}$=45.38	$\bar{x}$=45.62	$\bar{x}$=45.74	0.050
(discrete)	Abnormal Low	2.4%	3.0%	2.1%	0.930
	Normal	97.4%	96.7%	97.6%	
	Abnormal High	0.2%	0.3%	0.3%	
Platelet Count (thousand/mm^3)		(n=828)	(n=336)	(n=941)	
(continuous)[b]		$\bar{x}$=201.6	$\bar{x}$=205.5	$\bar{x}$=208.2	0.015
(discrete)	Abnormal Low	3.0%	3.6%	2.7%	0.860
	Normal	96.5%	95.8%	97.0%	
	Abnormal High	0.5%	0.6%	0.3%	
Prothrombin Time (seconds)		(n=667)	(n=271)	(n=766)	
(continuous)[a]		$\bar{x}$=10.53	$\bar{x}$=10.48	$\bar{x}$=10.46	0.215
(discrete)	High	2.0%	0.4%	1.2%	0.140
RBC Morphology		(n=834)	(n=338)	(n=943)	
	Abnormal	5.8%	9.5%	6.7%	0.072

Table F-7. Dependent Variable-Covariate Associations for the Hematology Assessment (Continued)

Dependent Variable	Level	Occupation: Officer	Enlisted Flyer	Enlisted Groundcrew	p-Value
Absolute Neutrophils		(n=834)	(n=338)	(n=943)	
(segs) (thousand/mm^3)[a]		$\bar{x}$ =3.60	$\bar{x}$ =3.94	$\bar{x}$ =4.00	<0.001
Absolute Neutrophils (bands) (thousand/mm^3)		(n=700)	(n=275)	(n=782)	
(continuous)[a]	Nonzero	$\bar{x}$ =0.186	$\bar{x}$ =0.198	$\bar{x}$ =0.201	0.179
(discrete)		(n=834)	(n=338)	(n=943)	
	Zero	16.1%	18.6%	17.1%	0.561
Absolute Lymphocytes		(n=834)	(n=338)	(x=943)	
(thousand/mm^3)[a]		$\bar{x}$ =1.68	$\bar{x}$ =1.75	$\bar{x}$ =1.82	<0.001
Absolute Monocytes		(n=834)	(n=338)	(n=943)	
(thousand/mm^3)[b]		$\bar{x}$ =0.468	$\bar{x}$ =0.491	$\bar{x}$ =0.486	0.119
Absolute Eosinophils (thousand/mm^3)		(n=753)	(n=299)	(n=804)	
(continuous)[a]	Nonzero	$\bar{x}$ =0.156	$\bar{x}$ =0.163	$\bar{x}$ =0.163	0.395
(discrete)		(n=834)	(n=338)	(n=943)	
	Zero	9.7%	11.5%	14.7%	0.005
Absolute Basophils (thousand/mm^3)		(n=381)	(n=162)	(n=410)	
(continuous)[a]	Nonzero	$\bar{x}$ =0.076	$\bar{x}$ =0.081	$\bar{x}$ =0.081	0.114
(discrete)		(n=834)	(n=338)	(n=943)	
	Zero	54.3%	52.1%	56.5%	0.332

Table F-7. Dependent Variable-Covariate Associations for the Hematology Assessment (Continued)

Dependent Variable	Level	Current Cigarette Smoking (cigarettes/day) 0-Never	0-Former	>0–20	>20	p-Value
RBC Count						
(million/mm³)		(n=593)	(n=1,116)	(n=268)	(n=137)	
(continuous)			r=0.064			0.003
(discrete)	Abnormal Low	4.1%	5.3%	6.0%	2.2%	0.627
	Normal	94.9%	93.8%	92.9%	97.1%	
	Abnormal High	1.0%	0.9%	1.1%	0.7%	
WBC Count						
(thousand/mm³)		(n=593)	(n=1,116)	(n=268)	(n=137)	
(continuous)[a]			r=0.395			<0.001
(discrete)	Abnormal Low	7.9%	5.2%	1.9%	1.5%	0.001
	Normal	90.7%	93.0%	88.4%	82.4%	
	Abnormal High	1.4%	1.8%	9.7%	16.1%	
Hemoglobin						
(gm/dl)		(n=593)	(n=1,116)	(n=268)	(n=137)	
(continuous)			r=0.213			<0.001
(discrete)	Abnormal Low	6.2%	8.1%	4.1%	2.2%	0.031
	Normal	93.5%	91.5%	94.8%	97.1%	
	Abnormal High	0.3%	0.4%	1.1%	0.7%	
Hematocrit						
(percent)		(n=593)	(n=1,116)	(n=268)	(n=137)	
(continuous)			r=0.209			<0.001
(discrete)	Abnormal Low	1.7%	3.0%	1.9%	1.5%	0.292
	Normal	98.1%	96.8%	97.3%	97.8%	
	Abnormal High	0.2%	0.2%	0.8%	0.7%	
Platelet Count						
(thousand/mm³)		(n=589)	(n=1,113)	(n=267)	(n=135)	
(continuous)[b]			r=0.062			0.005
(discrete)	Abnormal Low	2.9%	3.0%	3.4%	2.2%	0.070
	Normal	96.9%	96.6%	96.2%	95.6%	
	Abnormal High	0.2%	0.4%	0.4%	2.2%	
Prothrombin Time						
(seconds)			(n=1,703)			
(continuous)[a]			r=–0.025			0.298
(discrete)		(n=496)	(n=889)	(n=208)	(n=110)	
	High	1.2%	1.4%	1.9%	0.9%	0.862
RBC Morphology		(n=593)	(n=1,116)	(n=268)	(n=137)	
	Abnormal	3.7%	7.3%	9.7%	10.2%	0.001
Absolute Neutrophils			(n=2,114)			
(segs) (thousand/mm³)[a]			r=0.347			<0.001

Table F-7. Dependent Variable-Covariate Associations for the Hematology Assessment (Continued)

Dependent Variable	Level	Current Cigarette Smoking (cigarettes/day)				p-Value
		0-Never	0-Former	>0–20	>20	
Absolute Neutrophils (bands) (thousand/mm^3) (continuous) [a]	Nonzero		(n=1,756) r=0.188			<0.001
(discrete)	Zero	(n=593) 16.0%	(n=1,116) 17.8%	(n=268) 18.3%	(n=137) 11.0%	0.185
Absolute Lymphocytes (thousand/mm^3) [a]			(n=2,114) r=0.195			<0.001
Absolute Monocytes (thousand/mm^3) [b]			(n=2,114) r=0.160			<0.001
Absolute Eosinophils (thousand/mm^3) (continuous) [a]	Nonzero		(n=1,855) r=0.134			<0.001
(discrete)	Zero	(n=593) 12.8%	(n=1,116) 11.8%	(n=268) 11.6%	(n=137) 14.6%	0.758
Absolute Basophils (thousand/mm^3) (continuous) [a]	Nonzero		(n=953) r=0.267			<0.001
(discrete)	Zero	(n=593) 59.2%	(n=1,116) 52.5%	(n=268) 53.0%	(n=137) 59.9%	0.033

Table F-7. Dependent Variable-Covariate Associations for the Hematology Assessment (Continued)

Dependent Variable	Level	Lifetime Cigarette Smoking History (pack-years) 0	>0–10	>10	p-Value
RBC Count (million/mm^3)		(n=593)	(n=555)	(n=964)	
(continuous)			r=–0.047		0.031
(discrete)	Abnormal Low	4.1%	4.5%	5.5%	0.684
	Normal	94.9%	94.8%	93.5%	
	Abnormal High	1.0%	0.7%	1.0%	
WBC Count (thousand/mm^3)		(n=593)	(n=555)	(n=964)	
(continuous)[a]			r=0.236		<0.001
(discrete)	Abnormal Low	7.9%	5.8%	3.4%	0.001
	Normal	90.7%	91.1%	91.3%	
	Abnormal High	1.4%	3.1%	5.3%	
Hemoglobin (gm/dl)		(n=593)	(n=555)	(n=964)	
(continuous)			r=0.036		0.102
(discrete)	Abnormal Low	6.2%	5.2%	7.8%	0.304
	Normal	93.5%	94.4%	91.6%	
	Abnormal High	0.3%	0.4%	0.6%	
Hematocrit (percent)		(n=593)	(n=555)	(n=964)	
(continuous)			r=0.037		0.085
(discrete)	Abnormal Low	1.7%	2.0%	3.0%	0.134
	Normal	98.1%	98.0%	96.5%	
	Abnormal High	0.2%	0.0%	0.5%	
Platelet Count (thousand/mm^3)		(n=589)	(n=553)	(n=960)	
(continuous)[b]			r=0.094		<0.001
(discrete)	Abnormal Low	2.9%	2.7%	3.1%	0.123
	Normal	96.9%	97.3%	96.1%	
	Abnormal High	0.2%	0.0%	0.8%	
Prothrombin Time (seconds)			(n=1,702)		
(continuous)[a]			r=0.000		0.998
(discrete)		(n=496)	(n=438)	(n=768)	
	High	1.2%	1.1%	1.6%	0.788
RBC Morphology		(n=593)	(n=555)	(n=964)	
	Abnormal	3.7%	7.0%	8.5%	0.001
Absolute Neutrophils			(n=2,112)		
(segs) (thousand/mm^3)[a]			r=0.214		<0.001

Table F-7. Dependent Variable-Covariate Associations for the Hematology Assessment (Continued)

Dependent Variable	Level	Lifetime Cigarette Smoking History (pack-years) 0	>0–10	>10	p-Value
Absolute Neutrophils (bands) (thousand/mm^3) (continuous)[a]	Nonzero		(n=1,754) r=0.133		<0.001
(discrete)	Zero	(n=593) 16.0%	(n=555) 19.1%	(n=964) 16.3%	0.288
Absolute Lymphocytes (thousand/mm^3)[a]			(n=2,112) r=0.067		0.002
Absolute Monocytes (thousand/mm^3)[b]			(n=2,112) r=0.142		<0.001
Absolute Eosinophils (thousand/mm^3) (continuous)[a]	Nonzero		(n=1,853) r=0.086		<0.001
(discrete)	Zero	(n=593) 12.8%	(n=555) 10.6%	(n=964) 12.9%	0.393
Absolute Basophils (thousand/mm^3) (continuous)[a]	Nonzero		(n=952) r=0.168		<0.001
(discrete)	Zero	(n=593) 59.2%	(n=555) 54.4%	(n=964) 52.6%	0.038

[a] Analysis performed on natural logarithm scale; means transformed from natural logarithm scale.
[b] Analysis performed on square root scale; means transformed from square root scale.

Note: Correlations (r) are based on total sample size and are not category-specific.

Table F-8. Dependent Variable-Covariate Associations for the Endocrine Assessment

Dependent Variable	Level	Age: Born ≥1942	Age: Born <1942	Age: p-Value	Race: Black	Race: Non-Black	Race: p-Value
Past Thyroid Disease		(n=930)	(n=1,179)		(n=128)	(n=1,981)	
	Yes	6.5%	9.3%	0.020	6.3%	8.2%	0.543
Composite Diabetes Indicator		(n=920)	(n=1,171)		(n=125)	(n=1,966)	
	Diabetic	10.8%	21.8%	0.001	25.6%	16.4%	0.011
Diabetic Severity		(n=920)	(n=1,171)		(n=125)	(n=1,966)	
	Nondiabetic	90.5%	81.2%	0.001	76.0%	85.9%	0.023
	No Treat.	4.6%	6.2%		7.2%	5.4%	
	Diet Only	0.8%	2.5%		2.4%	1.7%	
	Oral Hypo.	2.9%	7.5%		11.2%	5.1%	
	Req. Insl.	1.2%	2.6%		3.2%	1.9%	
Time to Diabetes Onset		(n=2,091) $\beta=-0.014$		<0.001	(n=125) $\beta=-0.161$[a]	(n=1,966)	0.007
Thyroid Gland		(n=911)	(n=1,135)		(n=127)	(n=1,919)	
	Abnormal	0.7%	1.4%	0.155	0.0%	1.1%	0.442
Testicular Examination		(n=923)	(n=1,175)		(n=127)	(n=1,971)	
	Abnormal	1.4%	6.2%	0.001	3.1%	4.2%	0.744
TSH (μIU/ml)		(n=910)	(n=1,130)		(n=127)	(n=1,913)	
(continuous)[b]		r=0.133		<0.001	$\bar{x}=1.38$	$\bar{x}=1.87$	<0.001
(discrete)	Abn. Low	0.8%	1.1%	0.543	2.4%	0.8%	0.105
	Normal	96.0%	95.0%		96.1%	95.5%	
	Abn. High	3.2%	3.9%		1.6%	3.7%	
Thyroxine (μg/dl)		(n=910)	(n=1,130)		(n=127)	(n=1,913)	
(continuous)[c]		r=0.004		0.870	$\bar{x}=6.87$	$\bar{x}=7.07$	0.102
(discrete)	Low	2.4%	2.9%	0.576	3.9%	2.6%	0.543
Anti-Thyroid Antibodies		(n=910)	(n=1,130)		(n=127)	(n=1,913)	
	Present	0.7%	0.5%	0.932	0.0%	0.6%	0.767
Fasting Glucose (mg/dl)		(n=933)	(n=1,185)		(n=128)	(n=1,990)	
(continuous)[b]		r=0.142		<0.001	$\bar{x}=104.0$	$\bar{x}=101.5$	0.217
(discrete)	High	11.4%	21.8%	0.001	24.2%	16.7%	0.040
2-Hour Postprandial Glucose (μg/dl)		(n=821)	(n=916)		(n=93)	(n=1,644)	
(continuous)[b]		r=0.155		<0.001	$\bar{x}=101.8$	$\bar{x}=105.2$	0.265
(discrete)	Impaired	10.1%	20.9%	0.001	5.4%	16.4%	0.007
Fasting Urinary Glucose		(n=933)	(n=1,185)		(n=128)	(n=1,990)	
	Present	4.0%	4.4%	0.710	7.0%	4.0%	0.156
2-Hour Postprandial Urinary Glucose		(n=821)	(n=912)		(n=93)	(n=1,640)	
	Present	22.0%	24.3%	0.283	18.3%	23.5%	0.298

Table F-8. Dependent Variable-Covariate Associations for the Endocrine Assessment (Continued)

Dependent Variable	Level	Age: Born ≥1942	Age: Born <1942	Age: p-Value	Race: Black	Race: Non-Black	Race: p-Value
Serum Insulin (μIU/ml)		(n=821)	(n=916)		(n=93)	(n=1,644)	
(continuous) [b]		r=0.088		<0.001	$\bar{x}$=47.11	$\bar{x}$=47.98	0.847
(discrete)	Abn. Low	14.5%	11.5%	0.003	9.7%	13.1%	0.553
	Normal	47.9%	43.0%		49.5%	45.1%	
	Abn. High	37.6%	45.5%		40.9%	41.8%	
α-1-C Hemoglobin (percent)		(n=933)	(n=1,185)		(n=128)	(n=1,990)	
(continuous) [b]		r=0.098		<0.001	$\bar{x}$=7.07	$\bar{x}$=6.45	<0.001
(discrete)	High	8.1%	12.7%	0.001	25.8%	9.7%	0.001
Total Testosterone (ng/dl)		(n=916)	(n=1,161)		(n=126)	(n=1,951)	
(continuous) [c]		r=–0.131		<0.001	$\bar{x}$=418.2	$\bar{x}$=423.1	0.764
(discrete)	Low	7.2%	8.3%	0.415	7.1%	7.8%	0.911
Free Testosterone (pg/ml)		(n=916)	(n=1,611)		(n=126)	(n=1,951)	
(continuous) [c]		r=–0.368		<0.001	$\bar{x}$=13.83	$\bar{x}$=13.94	0.797
(discrete)	Low	0.5%	2.6%	0.001	2.4%	1.6%	0.788
Estradiol (pg/ml)		(n=933)	(n=1,188)		(n=128)	(n=1,993)	
(continuous) [c]		r=0.010		0.632	$\bar{x}$=44.26	$\bar{x}$=40.15	0.008
(discrete)	High	26.9%	28.2%	0.539	37.5%	27.0%	0.013
LH (mIU/ml)		(n=933)	(n=1,188)		(n=128)	(n=1,993)	
(continuous) [b]		r=0.185		<0.001	$\bar{x}$=3.82	$\bar{x}$=3.86	0.856
(discrete)	High	3.1%	7.6%	0.001	5.5%	5.6%	0.999
FSH (mIU/ml)		(n=933)	(n=1,188)		(n=128)	(n=1,993)	
(continuous) [b]		r=0.256		<0.001	$\bar{x}$=5.65	$\bar{x}$=6.03	0.255
(discrete)	High	4.0%	11.2%	0.001	8.6%	8.0%	0.936

Table F-8. Dependent Variable-Covariate Associations for the Endocrine Assessment (Continued)

Dependent Variable	Level	Occupation: Officer	Occupation: Enlisted Flyer	Occupation: Enlisted Groundcrew	p-Value
Past Thyroid Disease		(n=830)	(n=337)	(n=942)	
	Yes	9.0%	8.6%	7.0%	0.271
Composite Diabetes Indicator		(n=827)	(n=332)	(n=932)	
	Diabetic	14.9%	19.6%	17.8%	0.097
Diabetic Severity		(n=827)	(n=332)	(n=932)	
	Nondiabetic	86.5%	83.4%	85.0%	0.659
	No Treatment	5.0%	6.9%	5.5%	
	Diet Only	1.7%	1.2%	1.9%	
	Oral Hypoglycemic	4.6%	6.3%	6.0%	
	Requiring Insulin	2.3%	2.1%	1.6%	
Time to Diabetes Onset		(n=932)	(n=332)	(n=827)	
			β=–0.038 [d]	β=–0.052 [d]	0.159
Thyroid Gland		(n=798)	(n=326)	(n=922)	
	Abnormal	1.9%	0.6%	0.5%	0.019
Testicular Examination		(n=826)	(n=332)	(n=940)	
	Abnormal	5.2%	5.1%	2.8%	0.021
TSH (μIU/ml)		(n=794)	(n=326)	(n=920)	
(continuous) [b]		$\bar{x}$=1.94	$\bar{x}$=1.77	$\bar{x}$=1.78	0.007
(discrete)	Abnormal Low	0.8%	1.5%	0.9%	0.659
	Normal	95.3%	95.7%	95.5%	
	Abnormal High	3.9%	2.8%	3.6%	
Thyroxine (μg/dl)		(n=794)	(n=326)	(n=920)	
(continuous) [c]		$\bar{x}$=6.81	$\bar{x}$=7.26	$\bar{x}$=7.20	<0.001
(discrete)	Low	3.7%	1.8%	2.2%	0.099
Anti-Thyroid Antibodies		(n=794)	(n=326)	(n=920)	
	Present	0.8%	0.9%	0.3%	0.354
Fasting Glucose (mg/dl)		(n=833)	(n=338)	(n=947)	
(continuous) [b]		$\bar{x}$=100.4	$\bar{x}$=104.1	$\bar{x}$=101.8	0.039
(discrete)	High	15.7%	19.2%	17.7%	0.295
2-Hour Postprandial Glucose (mg/dl)		(n=704)	(n=267)	(n=766)	
(continuous) [b]		$\bar{x}$=103.5	$\bar{x}$=109.7	$\bar{x}$=104.8	0.014
(discrete)	Impaired	15.1%	19.9%	15.0%	0.139
Fasting Urinary Glucose		(n=833)	(n=338)	(n=947)	
	Present	2.8%	5.0%	5.2%	0.029
2-Hour Postprandial Urinary Glucose		(n=701)	(n=266)	(n=766)	
	Present	20.1%	26.7%	24.9%	0.033

Table F-8. Dependent Variable-Covariate Associations for the Endocrine Assessment (Continued)

Dependent Variable	Level	Occupation			
		Officer	Enlisted Flyer	Enlisted Groundcrew	p-Value
Serum Insulin (μIU/ml)		(n=704)	(n=267)	(n=766)	
(continuous) [b]		$\bar{x}$=43.67	$\bar{x}$=52.55	$\bar{x}$=50.58	0.001
(discrete)	Abnormal Low	14.9%	10.9%	11.7%	0.024
	Normal	47.7%	42.7%	44.0%	
	Abnormal High	37.4%	46.4%	44.3%	
α-1-C Hemoglobin (percent)		(n=833)	(n=338)	(n=947)	
(continuous) [b]		$\bar{x}$=6.33	$\bar{x}$=6.61	$\bar{x}$=6.58	<0.001
(discrete)	High	7.8%	13.6%	12.2%	0.002
Total Testosterone (ng/dl)		(n=815)	(n=328)	(n=934)	
(continuous) [c]		$\bar{x}$=410.7	$\bar{x}$=433.4	$\bar{x}$=429.7	0.043
(discrete)	Low	7.7%	7.0%	8.1%	0.804
Free Testosterone (pg/ml)		(n=815)	(n=328)	(n=934)	
(continuous) [c]		$\bar{x}$=13.12	$\bar{x}$=13.99	$\bar{x}$=14.65	<0.001
(discrete)	Low	2.1%	2.1%	1.2%	0.267
Estradiol (pg/ml)		(n=835)	(n=338)	(n=948)	
(continuous) [c]		$\bar{x}$=40.39	$\bar{x}$=41.66	$\bar{x}$=39.96	0.271
(discrete)	High	26.2%	30.5%	27.8%	0.331
LH (mIU/ml)		(n=835)	(n=338)	(n=948)	
(continuous) [b]		$\bar{x}$=3.93	$\bar{x}$=3.86	$\bar{x}$=3.80	0.553
(discrete)	High	6.2%	4.1%	5.6%	0.372
FSH (mIU/ml)		(n=835)	(n=338)	(n=948)	
(continuous) [b]		$\bar{x}$=6.31	$\bar{x}$=6.00	$\bar{x}$=5.75	0.008
(discrete)	High	10.4%	9.2%	5.5%	0.001

Table F-8. Dependent Variable-Covariate Associations for the Endocrine Assessment (Continued)

		Personality Type			Body Fat		
Dependent Variable	**Level**	**Type A**	**Type B**	**p-Value**	**Obese**	**Lean/Normal**	**p-Value**
Past Thyroid Disease		(n=816)	(n=1,290)				
	Yes	7.8%	8.2%	0.822	--	--	--
Composite Diabetes Indicator		(n=809)	(n=1,279)		(n=609)	(n=1,482)	
	Diabetic	13.0%	19.5%	0.001	28.6%	12.1%	0.001
Diabetic Severity		(n=809)	(n=1,279)		(n=609)	(n=1,482)	
	Nondiabetic	89.0%	83.0%	0.001	75.7%	89.3%	0.001
	No Treat.	4.3%	6.3%		9.9%	3.7%	
	Diet Only	1.1%	2.1%		2.1%	1.6%	
	Oral Hypo.	3.5%	6.8%		10.2%	3.6%	
	Req. Insulin	2.1%	1.9%		2.1%	1.9%	
Time to Diabetes Onset		(n=809)	(n=1,279)		(n=2,091)		
		β=0.129 [e]		<0.001	β=–0.024		<0.001
Thyroid Gland		(n=791)	(n=1,252)				
	Abnormal	0.9%	1.2%	0.654	--	--	--
Testicular Examination		(n=810)	(n=1,285)		(n=612)	(n=1,486)	
	Abnormal	3.8%	4.3%	0.692	2.8%	4.6%	0.066
TSH (μIU/ml)		(n=789)	(n=1,248)				
(continuous) [b]		$\bar{x}$=1.81	$\bar{x}$=1.85	0.423	--	--	--
(discrete)	Abn. Low	1.3%	0.7%	0.449	--	--	--
	Normal	95.1%	95.8%				
	Abn. High	3.7%	3.5%				
Thyroxine (μg/dl)		(n=789)	(n=1,248)				
(continuous) [c]		$\bar{x}$=7.02	$\bar{x}$=7.08	0.368	--	--	--
(discrete)	Low	2.2%	3.0%	0.286	--	--	--
Anti-Thyroid Antibodies		(n=789)	(n=1,248)				
	Present	0.6%	0.6%	0.999	--	--	--
Fasting Glucose (mg/dl)		(n=817)	(n=1,298)		(n=620)	(n=1,498)	
(continuous) [b]		$\bar{x}$=99.6	$\bar{x}$=102.9	0.001	r=0.212		<0.001
(discrete)	High	13.6%	19.4%	0.001	26.8%	13.2%	0.001
2-Hour Postprandial Glucose (mg/dl)		(n=704)	(n=1,030)		(n=435)	(n=1,302)	
(continuous) [b]		$\bar{x}$=103.3	$\bar{x}$=106.3	0.035	r=0.282		<0.001
(discrete)	Impaired	16.1%	15.6%	0.866	27.4%	11.9%	0.001
Fasting Urinary Glucose		(n=817)	(n=1,298)		(n=620)	(n=1,498)	
	Present	2.6%	5.2%	0.004	6.8%	3.1%	0.001
2-Hour Postprandial Urinary Glucose		(n=703)	(n=1,027)		(n=433)	(n=1,300)	
	Present	23.0%	23.5%	0.884	24.7%	22.8%	0.446

Table F-8. Dependent Variable-Covariate Associations for the Endocrine Assessment (Continued)

Dependent Variable	Level	Personality Type: Type A	Type B	p-Value	Body Fat: Obese	Lean/Normal	p-Value
Serum Insulin (μIU/ml)		(n=704)	(n=1,030)		(n=435)	(n=1,302)	
(continuous) [b]		$\bar{x}$=44.72	$\bar{x}$=50.42	0.006	r=0.433		<0.001
(discrete)	Abn. Low	14.9%	11.4%	0.018	2.5%	16.4%	0.001
	Normal	46.7%	44.5%		26.4%	51.6%	
	Abn. High	38.4%	44.2%		71.0%	32.0%	
α-1-C Hemoglobin (percent)		(n=817)	(n=1,298)		(n=620)	(n=1,498)	
(continuous) [b]		$\bar{x}$=6.36	$\bar{x}$=6.57	<0.001	r=0.227		<0.001
(discrete)	High	7.5%	12.8%	0.001	17.4%	7.9%	0.001
Total Testosterone (ng/dl)		(n=800)	(n=1,274)		(n=607)	(n=1,470)	
(continuous) [c]		$\bar{x}$=432.2	$\bar{x}$=417.1	0.059	r=–0.382		<0.001
(discrete)	Low	7.5%	7.9%	0.787	15.3%	4.7%	0.001
Free Testosterone (pg/ml)		(n=800)	(n=1,274)		(n=607)	(n=1,470)	
(continuous) [c]		$\bar{x}$=14.37	$\bar{x}$=13.68	0.001	r=–0.272		<0.001
(discrete)	Low	1.0%	2.1%	0.080	3.1%	1.1%	0.002

Dependent Variable	Level	Family History of Diabetes: Yes	No	p-Value
Composite Diabetes Indicator	Diabetic	(n=547) 24.9%	(n=1,525) 14.1%	0.001
Diabetic Severity		(n=547)	(n=1,525)	
	Nondiabetic	77.7%	88.0%	0.001
	No Treatment	7.5%	4.8%	
	Diet Only	2.2%	1.6%	
	Oral Hypoglycemic	9.1%	4.3%	
	Requiring Insulin	3.5%	1.4%	
Time to Diabetes Onset		(n=547)	(n=1,544)	
		β=–0.196 [f]		<0.001
Fasting Glucose (mg/dl)		(n=556)	(n=1,543)	
(continuous) [b]		$\bar{x}$=107.1	$\bar{x}$=99.8	<0.001
(discrete)	High	25.2%	14.4%	0.001
2-Hour Postprandial Glucose (mg/dl)		(n=411)	(n=1,310)	
(continuous) [b]		$\bar{x}$=108.9	$\bar{x}$=104.0	0.003
(discrete)	Impaired	19.5%	14.7%	0.024

Table F-8. Dependent Variable-Covariate Associations for the Endocrine Assessment (Continued)

Dependent Variable	Level	Family History of Diabetes		p-Value
		Yes	No	
Fasting Urinary Glucose		(n=556)	(n=1,543)	
	Present	6.1%	3.5%	0.012
2-Hour Postprandial Urinary Glucose		(n=411)	(n=1,306)	
	Present	25.1%	22.7%	0.349
Serum Insulin (μIU/ml)		(n=411)	(n=1,310)	
(continuous) [b]		$\bar{x}$=54.32	$\bar{x}$=46.28	0.001
(discrete)	Abnormal Low	8.5%	14.2%	0.001
	Normal	41.8%	46.4%	
	Abnormal High	49.6%	39.4%	
α-1-C Hemoglobin (percent)		(n=556)	(n=1,543)	
(continuous) [b]		$\bar{x}$=6.73	$\bar{x}$=6.40	<0.001
(discrete)	High	16.0%	8.8%	0.001

[a] Estimated coefficient relative to non-Blacks.
[b] Analysis performed on natural logarithm scale; means transformed from natural logarithm scale.
[c] Analysis performed on square root scale; means transformed from square root scale.
[d] Estimated coefficient relative to officers.
[e] Estimated coefficient relative to personality type B.
[f] Estimated coefficient relative to no family history of diabetes.
--: Covariate not applicable for dependent variable.

Note: Correlations (r) are based on total sample size and are not category-specific.

Table F-9. Dependent Variable-Covariate Associations for the Immunologic Assessment

Dependent Variable	Level	Age: Born ≥1942	Age: Born <1942	Age: p-Value	Race: Black	Race: Non-Black	Race: p-Value
CD3+ Cells (T Cells) (cells/mm^3)[a]		(n=774) r=–0.099		0.006	(n=46) $\bar{x}$=1,363.1	(n=728) $\bar{x}$=1,239.6	0.095
CD4+ Cells (Helper T Cells) (cells/mm^3)[a]		(n=774) r=–0.140		<0.001	(n=46) $\bar{x}$=958.7	(n=728) $\bar{x}$=844.4	0.023
CD8+ Cells (Suppressor T Cells) (cells/mm^3)[a]		(n=774) r=0.007		0.845	(n=46) $\bar{x}$=621.4	(n=728) $\bar{x}$=575.0	0.278
CD16+56+ Cells (Natural Killer Cells) (cells/mm^3)[a]		(n=774) r=0.102		0.005	(n=46) $\bar{x}$=288.1	(n=728) $\bar{x}$=267.7	0.326
CD20+ Cells (B Cells) (cells/mm^3)[a]		(n=773) r=–0.240		<0.001	(n=46) $\bar{x}$=232.9	(n=727) $\bar{x}$=182.2	0.007
CD3+CD4+ Cells (Helper T Cells) (cells/mm^3)[a]		(n=774) r=–0.142		<0.001	(n=46) $\bar{x}$=860.6	(n=728) $\bar{x}$=770.2	0.061
Absolute Lymphocytes (cells/mm^3)[a]		(n=2,029) r=–0.097		<0.001	(n=125) $\bar{x}$=1,879.4	(n=1,904) $\bar{x}$=1,772.9	0.070
IgA (mg/dl)[a]		(n=2,029) r=0.056		0.012	(n=125) $\bar{x}$=247.6	(n=1,904) $\bar{x}$=232.0	0.142
IgG (mg/dl)[a]		(n=2,029) r=0.021		0.337	(n=125) $\bar{x}$=1,266.8	(n=1,904) $\bar{x}$=1,029.2	<0.001
IgM (mg/dl)[a]		(n=2,029) r=–0.063		0.005	(n=125) $\bar{x}$=85.4	(n=1,904) $\bar{x}$=98.4	0.004
Lupus Panel: ANA Test	Present	(n=905) 49.9%	(n=1,124) 53.7%	0.098	(n=125) 47.2%	(n=1,904) 52.4%	0.304
Lupus Panel: ANA Thyroid Microsomal Antibody	Present	(n=905) 2.4%	(n=1,124) 3.2%	0.366	(n=125) 4.0%	(n=1,904) 2.8%	0.608
Lupus Panel: MSK Smooth Muscle Antibody	Present	(n=905) 11.9%	(n=1,124) 12.3%	0.867	(n=125) 19.2%	(n=1,904) 11.7%	0.018
Lupus Panel: MSK Mitochondrial Antibody	Present	(n=905) 0.2%	(n=1,124) 0.4%	0.885	(n=125) 0.0%	(n=1,904) 0.3%	0.999
Lupus Panel: MSK Parietal Antibody	Present	(n=905) 3.9%	(n=1,124) 4.6%	0.466	(n=125) 10.4%	(n=1,904) 3.9%	0.001
Lupus Panel: Rheumatoid Factor	Present	(n=905) 9.5%	(n=1,124) 12.2%	0.064	(n=125) 11.2%	(n=1,904) 11.0%	0.999

Table F-9. Dependent Variable-Covariate Associations for the Immunologic Assessment (Continued)

Dependent Variable	Level	Occupation: Officer	Enlisted Flyer	Enlisted Groundcrew	p-Value
CD3+ Cells (T Cells) (cells/mm³)[a]		(n=299) $\bar{x}$=1,208.0	(n=134) $\bar{x}$=1,248.6	(n=341) $\bar{x}$=1,280.7	0.142
CD4+ Cells (Helper T Cells) (cells/mm³)[a]		(n=299) $\bar{x}$=830.7	(n=134) $\bar{x}$=843.9	(n=341) $\bar{x}$=871.7	0.246
CD8+ Cells (Suppressor T Cells) (cells/mm³)[a]		(n=299) $\bar{x}$=554.9	(n=134) $\bar{x}$=599.1	(n=341) $\bar{x}$=590.0	0.159
CD16+56+ Cells (Natural Killer Cells) (cells/mm³)[a]		(n=299) $\bar{x}$=271.6	(n=134) $\bar{x}$=266.5	(n=341) $\bar{x}$=267.5	0.901
CD20+ Cells (B Cells) (cells/mm³)[a]		(n=298) $\bar{x}$=170.8	(n=134) $\bar{x}$=178.8	(n=341) $\bar{x}$=200.9	0.002
CD3+CD4+ Cells (Helper T Cells) (cells/mm³)[a]		(n=299) $\bar{x}$=755.7	(n=134) $\bar{x}$=768.6	(n=341) $\bar{x}$=795.7	0.236
Absolute Lymphocytes (cells/mm³)[a]		(n=802) $\bar{x}$=1,703.3	(n=320) $\bar{x}$=1,788.5	(n=907) $\bar{x}$=1,845.8	<0.001
IgA (mg/dl)[a]		(n=802) $\bar{x}$=225.0	(n=320) $\bar{x}$=237.3	(n=907) $\bar{x}$=238.7	0.030
IgG (mg/dl)[a]		(n=802) $\bar{x}$=1,026.7	(n=320) $\bar{x}$=1,036.8	(n=907) $\bar{x}$=1,058.6	0.019
IgM (mg/dl)[a]		(n=802) $\bar{x}$=95.6	(n=320) $\bar{x}$=99.9	(n=907) $\bar{x}$=98.4	0.360
Lupus Panel: ANA Test	Present	(n=802) 52.2%	(n=320) 50.0%	(n=907) 52.6%	0.720
Lupus Panel: ANA Thyroid Microsomal Antibody	Present	(n=802) 3.1%	(n=320) 2.5%	(n=907) 2.8%	0.829
Lupus Panel: MSK Smooth Muscle Antibody	Present	(n=802) 11.5%	(n=320) 12.8%	(n=907) 12.5%	0.756
Lupus Panel: MSK Mitochondrial Antibody	Present	(n=802) 0.6%	(n=320) 0.3%	(n=907) 0.0%	0.060
Lupus Panel: MSK Parietal Antibody	Present	(n=802) 3.6%	(n=320) 4.7%	(n=907) 4.7%	0.482
Lupus Panel: Rheumatoid Factor	Present	(n=802) 12.3%	(n=320) 13.1%	(n=907) 9.0%	0.038

Table F-9. Dependent Variable-Covariate Associations for the Immunologic Assessment (Continued)

Dependent Variable	Level	Current Cigarette Smoking (cigarettes/day) 0-Never	0-Former	>0–20	>20	p-Value
CD3+ Cells (T Cells) (cells/mm³)[a]			(n=773) r=0.233			<0.001
CD4+ Cells (Helper T Cells) (cells/mm³)[a]			(n=773) r=0.242			<0.001
CD8+ Cells (Suppressor T Cells) (cells/mm³)[a]			(n=773) r=0.126			<0.001
CD16+56+ Cells (Natural Killer Cells) (cells/mm³)[a]			(n=773) r=–0.169			<0.001
CD20+ Cells (B Cells) (cells/mm³)[a]			(n=772) r=0.151			<0.001
CD3+CD4+ Cells (Helper T Cells) (cells/mm³)[a]			(n=773) r=0.257			<0.001
Absolute Lymphocytes (cells/mm³)[a]			(n=2,028) r=0.190			<0.001
IgA (mg/dl)[a]			(n=2,028) r=–0.016			0.460
IgG (mg/dl)[a]			(n=2,028) r=–0.114			<0.001
IgM (mg/dl)[a]			(n=2,028) r=0.014			0.532
Lupus Panel: ANA Test		(n=571)	(n=1,060)	(n=261)	(n=136)	
	Present	50.8%	49.1%	63.2%	59.6%	0.001
Lupus Panel: ANA Thyroid		(n=571)	(n=1,060)	(n=261)	(n=136)	
Microsomal Antibody	Present	3.2%	3.2%	1.5%	1.5%	0.357
Lupus Panel: MSK Smooth		(n=571)	(n=1,060)	(n=261)	(n=136)	
Muscle Antibody	Present	11.0%	11.9%	17.2%	8.8%	0.037
Lupus Panel: MSK		(n=571)	(n=1,060)	(n=261)	(n=136)	
Mitochondrial Antibody	Present	0.4%	0.2%	0.4%	0.7%	0.699
Lupus Panel: MSK Parietal		(n=571)	(n=1,060)	(n=261)	(n=136)	
Antibody	Present	3.9%	4.3%	4.6%	5.9%	0.760
Lupus Panel: Rheumatoid		(n=571)	(n=1,060)	(n=261)	(n=136)	
Factor	Present	11.6%	10.5%	11.5%	11.8%	0.889

Table F-9. Dependent Variable-Covariate Associations for the Immunologic Assessment (Continued)

Dependent Variable	Level	Lifetime Cigarette Smoking History (pack-years) 0	>0–10	>10	p-Value
CD3+ Cells (T Cells) (cells/mm^3)[a]			(n=772) r=0.058		0.109
CD4+ Cells (Helper T Cells) (cells/mm^3)[a]			(n=772) r=0.070		0.053
CD8+ Cells (Suppressor T Cells) (cells/mm^3)[a]			(n=772) r=0.016		0.650
CD16+56+ Cells (Natural Killer Cells) (cells/mm^3)[a]			(n=772) r=–0.054		0.132
CD20+ Cells (B Cells) (cells/mm^3)[a]			(n=771) r=0.018		0.613
CD3+CD4+ Cells (Helper T Cells) (cells/mm^3)[a]			(n=772) r=0.077		0.032
Absolute Lymphocytes (cells/mm^3)[a]			(n=2,027) r=0.091		<0.001
IgA (mg/dl)[a]			(n=2,027) r=0.018		0.413
IgG (mg/dl)[a]			(n=2,027) r=–0.105		<0.001
IgM (mg/dl)[a]			(n=2,027) r=0.034		0.131
Lupus Panel: ANA Test		(n=571)	(n=540)	(n=916)	
	Present	50.8%	48.3%	55.1%	0.033
Lupus Panel: ANA Thyroid		(n=571)	(n=540)	(n=916)	
Microsomal Antibody	Present	3.2%	3.7%	2.2%	0.216
Lupus Panel: MSK Smooth		(n=571)	(n=540)	(n=916)	
Muscle Antibody	Present	11.0%	11.1%	13.4%	0.270
Lupus Panel: MSK		(n=571)	(n=540)	(n=916)	
Mitochondrial Antibody	Present	0.4%	0.0%	0.4%	0.321
Lupus Panel: MSK Parietal		(n=571)	(n=540)	(n=916)	
Antibody	Present	3.9%	5.2%	4.0%	0.482
Lupus Panel: Rheumatoid		(n=571)	(n=540)	(n=916)	
Factor	Present	11.6%	7.4%	12.8%	0.006

Table F-9. Dependent Variable-Covariate Associations for the Immunologic Assessment (Continued)

Dependent Variable	Level	Current Alcohol Use (drinks/day) 0–1	>1–4	>4	p-Value
CD3+ Cells (T Cells) (cells/mm^3)[a]			(n=773) r=0.029		0.415
CD4+ Cells (Helper T Cells) (cells/mm^3)[a]			(n=773) r=0.042		0.249
CD8+ Cells (Suppressor T Cells) (cells/mm^3)[a]			(n=773) r=–0.007		0.854
CD16+56+ Cells (Natural Killer Cells) (cells/mm^3)[a]			(n=773) r=–0.045		0.214
CD20+ Cells (B Cells) (cells/mm^3)[a]			(n=772) r=–0.097		0.007
CD3+CD4+ Cells (Helper T Cells) (cells/mm^3)[a]			(n=773) r=0.044		0.225
Absolute Lymphocytes (cells/mm^3)[a]			(n=2,028) r=0.010		0.649
IgA (mg/dl)[a]			(n=2,028) r=0.048		0.032
IgG (mg/dl)[a]			(n=2,028) r=–0.084		<0.001
IgM (mg/dl)[a]			(n=2,028) r=0.057		0.010
Lupus Panel: ANA Test		(n=1,628)	(n=352)	(n=48)	
	Present	51.0%	56.0%	60.4%	0.119
Lupus Panel: ANA Thyroid		(n=1,628)	(n=352)	(n=48)	
Microsomal Antibody	Present	3.0%	2.6%	0.0%	0.436
Lupus Panel: MSK Smooth Muscle		(n=1,628)	(n=352)	(n=48)	
Antibody	Present	11.9%	13.1%	12.5%	0.833
Lupus Panel: MSK Mitochondrial		(n=1,628)	(n=352)	(n=48)	
Antibody	Present	0.4%	0.0%	0.0%	0.477
Lupus Panel: MSK Parietal		(n=1,628)	(n=352)	(n=48)	
Antibody	Present	4.5%	4.0%	0.0%	0.304
Lupus Panel: Rheumatoid Factor		(n=1,628)	(n=352)	(n=48)	
	Present	10.9%	10.5%	18.8%	0.217

Table F-9. Dependent Variable-Covariate Associations for the Immunologic Assessment (Continued)

Dependent Variable	Level	Lifetime Alcohol History (drink-years) 0	>0-40	>40	p-Value
CD3+ Cells (T Cells) (cells/mm^3)[a]			(n=772) r=0.042		0.244
CD4+ Cells (Helper T Cells) (cells/mm^3)[a]			(n=772) r=0.055		0.124
CD8+ Cells (Suppressor T Cells) (cells/mm^3)[a]			(n=772) r=–0.005		0.898
CD16+56+ Cells (Natural Killer Cells) (cells/mm^3)[a]			(n=772) r=–0.051		0.154
CD20+ Cells (B Cells) (cells/mm^3)[a]			(n=771) r=–0.038		0.287
CD3+CD4+ Cells (Helper T Cells) (cells/mm^3)[a]			(n=772) r=0.059		0.104
Absolute Lymphocytes (cells/mm^3)[a]			(n=2,021) r=0.009		0.678
IgA (mg/dl)[a]			(n=2,021) r=0.038		0.086
IgG (mg/dl)[a]			(n=2,021) r=–0.060		0.007
IgM (mg/dl)[a]			(n=2,021) r=0.005		0.835
Lupus Panel: ANA Test		(n=112)	(n=1,324)	(n=585)	
	Present	49.1%	51.1%	54.7%	0.279
Lupus Panel: ANA Thyroid		(n=112)	(n=1,324)	(n=585)	
Microsomal Antibody	Present	1.8%	3.0%	2.6%	0.680
Lupus Panel: MSK Smooth		(n=112)	(n=1,324)	(n=585)	
Muscle Antibody	Present	15.2%	11.6%	12.7%	0.488
Lupus Panel: MSK		(n=112)	(n=1,324)	(n=585)	
Mitochondrial Antibody	Present	0.0%	0.4%	0.2%	0.625
Lupus Panel: MSK Parietal		(n=112)	(n=1,324)	(n=585)	
Antibody	Present	6.3%	4.7%	2.9%	0.116
Lupus Panel: Rheumatoid		(n=112)	(n=1,324)	(n=585)	
Factor	Present	11.6%	10.5%	12.0%	0.625

Table F-9. Dependent Variable-Covariate Associations for the Immunologic Assessment (Continued)

Dependent Variable	Level	Physical Activity Index: Active	Moderate	Sedentary	p-Value
CD3+ Cells (T Cells) (cells/mm³)[a]		(n=202)	(n=149)	(n=418)	
		$\bar{x}$=1,168.8	$\bar{x}$=1,174.1	$\bar{x}$=1,315.1	<0.001
CD4+ Cells (Helper T Cells) (cells/mm³)[a]		(n=202)	(n=149)	(n=418)	
		$\bar{x}$=807.1	$\bar{x}$=806.8	$\bar{x}$=889.2	0.001
CD8+ Cells (Suppressor T Cells) (cells/mm³)[a]		(n=202)	(n=149)	(n=418)	
		$\bar{x}$=548.3	$\bar{x}$=539.1	$\bar{x}$=608.3	0.005
CD16+56+ Cells (Natural Killer Cells) (cells/mm³)[a]		(n=202)	(n=149)	(n=418)	
		$\bar{x}$=267.5	$\bar{x}$=269.4	$\bar{x}$=268.8	0.990
CD20+ Cells (B Cells) (cells/mm³)[a]		(n=201)	(n=149)	(n=418)	
		$\bar{x}$=168.2	$\bar{x}$=183.1	$\bar{x}$=194.9	0.017
CD3+CD4+ Cells (Helper T Cells) (cells/mm³)[a]		(n=202)	(n=149)	(n=418)	
		$\bar{x}$=732.5	$\bar{x}$=728.9	$\bar{x}$=814.3	0.001
Absolute Lymphocytes (cells/mm³)[a]		(n=539)	(n=400)	(n=1,077)	
		$\bar{x}$=1,719.7	$\bar{x}$=1,722.7	$\bar{x}$=1,831.0	<0.001
IgA (mg/dl)[a]		(n=539)	(n=400)	(n=1,077)	
		$\bar{x}$=231.8	$\bar{x}$=223.1	$\bar{x}$=237.2	0.088
IgG (mg/dl)[a]		(n=539)	(n=400)	(n=1,077)	
		$\bar{x}$=1,040.4	$\bar{x}$=1,030.0	$\bar{x}$=1,047.1	0.457
IgM (mg/dl)[a]		(n=539)	(n=400)	(n=1,077)	
		$\bar{x}$=99.8	$\bar{x}$=94.8	$\bar{x}$=97.5	0.344
Lupus Panel: ANA Test		(n=539)	(n=400)	(n=1,077)	
	Present	48.6%	52.5%	53.5%	0.176
Lupus Panel: ANA Thyroid Microsomal Antibody		(n=539)	(n=400)	(n=1,077)	
	Present	1.7%	4.3%	2.9%	0.061
Lupus Panel: MSK Smooth Muscle Antibody		(n=539)	(n=400)	(n=1,077)	
	Present	9.5%	13.5%	12.9%	0.085
Lupus Panel: MSK Mitochondrial Antibody		(n=539)	(n=400)	(n=1,077)	
	Present	0.4%	0.8%	0.1%	0.112
Lupus Panel: MSK Parietal Antibody		(n=539)	(n=400)	(n=1,077)	
	Present	3.9%	4.3%	4.5%	0.871
Lupus Panel: Rheumatoid Factor		(n=539)	(n=400)	(n=1,077)	
	Present	10.2%	9.5%	12.0%	0.314

[a] Analysis performed on natural logarithm scale; means transformed from natural logarithm scale.

Note: Correlations (r) are based on total sample size and are not category-specific.

Table F-10. Dependent Variable-Covariate Associations for the Pulmonary Assessment

Dependent Variable	Level	Age: Born ≥1942	Age: Born <1942	Age: p-Value	Race: Black	Race: Non-Black	Race: p-Value
Asthma		(n=928)	(n=1,177)		(n=127)	(n=1,978)	
	Yes	3.9%	4.2%	0.828	3.1%	4.1%	0.770
Bronchitis		(n=922)	(n=1,148)		(n=126)	(n=1,944)	
	Yes	19.8%	20.5%	0.768	13.5%	20.6%	0.069
Pneumonia		(n=917)	(n=1,113)		(n=125)	(n=1,905)	
	Yes	8.6%	13.1%	0.002	12.8%	11.0%	0.628
Thorax and Lung		(n=933)	(n=1,188)		(n=128)	(n=1,993)	
Abnormalities	Yes	8.6%	13.6%	0.001	5.5%	11.8%	0.042
X-ray Interpretation		(n=931)	(n=1,188)		(n=128)	(n=1,991)	
	Abnormal	8.4%	11.6%	0.018	6.3%	10.4%	0.171
FVC		(n=2,118)			(n=128)	(n=1,990)	
		r=–0.035		0.108	$\bar{x}$=87.84	$\bar{x}$=99.81	<0.001
FEV_1		(n=2,118)			(n=128)	(n=1,990)	
		r=–0.143		<0.001	$\bar{x}$=86.83	$\bar{x}$=94.71	<0.001
Ratio of Observed FEV_1 to Observed FVC[a]		(n=2,118)			(n=128)	(n=1,990)	
		r=0.266		<0.001	$\bar{x}$=0.791	$\bar{x}$=0.760	<0.001
Loss of Vital Capacity		(n=931)	(n=1,187)		(n=128)	(n=1,990)	
	None	92.3%	89.6%	0.031	78.1%	91.6%	0.001
	Mild	7.0%	8.4%		17.2%	7.2%	
	Mod./Sev.	0.8%	1.9%		4.7%	1.2%	
Obstructive		(n=931)	(n=1,187)		(n=128)	(n=1,990)	
Abnormality	None	75.1%	52.1%	0.001	63.3%	62.2%	0.938
	Mild	21.9%	37.1%		30.5%	30.4%	
	Moderate	2.6%	8.6%		4.7%	6.0%	
	Severe	0.4%	2.2%		1.6%	1.4%	

Table F-10. Dependent Variable-Covariate Associations for the Pulmonary Assessment (Continued)

Dependent Variable	Level	Occupation: Officer	Enlisted Flyer	Enlisted Groundcrew	p-Value
Asthma		(n=830)	(n=336)	(n=939)	
	Yes	4.2%	3.3%	4.2%	0.738
Bronchitis		(n=811)	(n=327)	(n=932)	
	Yes	18.0%	22.9%	21.1%	0.108
Pneumonia		(n=792)	(n=319)	(n=919)	
	Yes	12.4%	10.7%	10.1%	0.323
Thorax and Lung		(n=835)	(n=338)	(n=948)	
Abnormalities	Yes	7.7%	18.6%	12.1%	0.001
X-ray Interpretation		(n=835)	(n=338)	(n=946)	
	Abnormal	9.7%	9.8%	10.8%	0.723
FVC		(n=835)	(n=337)	(n=946)	
		$\bar{x}$=100.28	$\bar{x}$=99.22	$\bar{x}$=97.99	0.005
FEV_1		(n=835)	(n=337)	(n=946)	
		$\bar{x}$=95.57	$\bar{x}$=91.76	$\bar{x}$=93.90	0.002
Ratio of Observed FEV_1 to Observed FVC[a]		(n=835)	(n=337)	(n=946)	
		$\bar{x}$=0.759	$\bar{x}$=0.745	$\bar{x}$=0.771	<0.001
Loss of Vital		(n=835)	(n=337)	(n=946)	
Capacity	None	92.1%	89.9%	90.0%	0.587
	Mild	6.7%	8.6%	8.5%	
	Moderate/Severe	1.2%	1.5%	1.6%	
Obstructive		(n=835)	(n=337)	(n=946)	
Abnormality	None	61.0%	53.1%	66.6%	0.001
	Mild	32.5%	35.9%	26.6%	
	Moderate	5.4%	7.7%	5.8%	
	Severe	1.2%	3.3%	1.0%	

Table F-10. Dependent Variable-Covariate Associations for the Pulmonary Assessment (Continued)

Dependent Variable	Level	Current Cigarette Smoking (cigarettes/day) 0-Never	0-Former	>0–20	>20	p-Value
Asthma						
	Yes	--	--	--	--	--
Bronchitis						
	Yes	--	--	--	--	--
Pneumonia						
	Yes	--	--	--	--	--
Thorax and Lung Abnormalities	Yes	(n=595) 2.2%	(n=1,116) 7.9%	(n=272) 29.8%	(n=137) 43.8%	0.001
X-ray Interpretation	Abnormal	(n=595) 8.4%	(n=1,115) 10.7%	(n=272) 10.3%	(n=136) 14.0%	0.214
FVC			(n=2,117) r=–0.068			0.002
FEV_1			(n=2,117) r=–0.208			<0.001
Ratio of Observed FEV_1 to Observed FVC[a]			(n=2,117) r=0.222			<0.001
Loss of Vital Capacity		(n=595)	(n=1,115)	(n=270)	(n=137)	
	None	92.9%	90.9%	86.7%	88.3%	0.116
	Mild	6.1%	7.5%	11.5%	10.2%	
	Moderate/Severe	1.0%	1.5%	1.9%	1.5%	
Obstructive Abnormality		(n=595)	(n=1,115)	(n=270)	(n=137)	
	None	78.0%	60.8%	45.9%	38.0%	0.001
	Mild	20.0%	31.4%	40.7%	46.7%	
	Moderate	1.7%	6.3%	10.4%	13.1%	
	Severe	0.3%	1.5%	3.0%	2.2%	

Table F-10. Dependent Variable-Covariate Associations for the Pulmonary Assessment (Continued)

Dependent Variable	Level	Lifetime Cigarette Smoking History (pack-years)			
		0	>0–10	>10	p-Value
Asthma		(n=590)	(n=553)	(n=959)	
	Yes	4.1%	4.5%	3.6%	0.703
Bronchitis		(n=582)	(n=545)	(n=940)	
	Yes	16.8%	18.0%	23.5%	0.002
Pneumonia		(n=575)	(n=538)	(n=914)	
	Yes	9.6%	9.3%	13.0%	0.037
Thorax and Lung		(n=595)	(n=558)	(n=965)	
Abnormalities	Yes	2.2%	8.1%	19.0%	0.001
X-ray Interpretation		(n=595)	(n=557)	(n=964)	
	Yes	8.4%	8.6%	12.2%	0.018
FVC			(n=2,115)		
			r=–0.145		<0.001
FEV_1			(n=2,115)		
			r=–0.302		<0.001
Ratio of Observed FEV_1 to Observed FVC[a]			(n=2,115)		
			r=0.291		<0.001
Loss of Vital		(n=595)	(n=556)	(n=964)	
Capacity	None	92.9%	92.4%	88.6%	0.029
	Mild	6.1%	6.3%	9.6%	
	Moderate/Severe	1.0%	1.3%	1.8%	
Obstructive		(n=595)	(n=556)	(n=964)	
Abnormality	None	78.0%	68.7%	49.0%	0.001
	Mild	20.0%	27.0%	38.8%	
	Moderate	1.7%	3.4%	9.9%	
	Severe	0.3%	0.9%	2.4%	

Table F-10. Dependent Variable-Covariate Associations for the Pulmonary Assessment (Continued)

Dependent Variable	Level	Body Fat			Industrial Chemical Exposure		
		Normal	Obese	p-Value	No	Yes	p-Value
Asthma		(n=1,489)	(n=616)		(n=801)	(n=1,304)	
	Yes	4.0%	4.1%	0.999	3.9%	4.1%	0.847
Bronchitis		(n=1,464)	(n=606)		(n=786)	(n=1,284)	
	Yes	20.2%	20.3%	0.988	17.2%	22.0%	0.009
Pneumonia		(n=1,437)	(n=593)		(n=765)	(n=1,265)	
	Yes	10.9%	11.5%	0.783	11.4%	10.9%	0.803
Thorax and Lung		(n=1,501)	(n=620)		(n=804)	(n=1,317)	
Abnormalities	Yes	12.3%	9.2%	0.047	9.7%	12.5%	0.062
X-ray Interpretation		(n=1,499)	(n=620)		(n=804)	(n=1,315)	
	Abnormal	10.1%	10.5%	0.837	10.2%	10.2%	0.999
FVC		(n=2,118)			(n=803)	(n=1,315)	
		r=–0.224		<0.001	$\bar{x}$=99.77	$\bar{x}$=98.67	0.102
FEV_1		(n=2,118)			(n=803)	(n=1,315)	
		r=–0.070		0.001	$\bar{x}$=95.04	$\bar{x}$=93.72	0.092
Ratio of Observed FEV_1 to Observed FVC[a]		(n=2,118)			(n=803)	(n=1,315)	
		r=–0.178		<0.001	$\bar{x}$=0.761	$\bar{x}$=0.763	0.587
Loss of Vital		(n=1,498)	(n=620)		(n=803)	(n=1,315)	
Capacity	None	92.9%	85.8%	0.001	92.5%	89.7%	0.064
	Mild	6.1%	11.9%		6.6%	8.5%	
	Mod./Severe	1.1%	2.3%		0.9%	1.7%	
Obstructive		(n=1,498)	(n=620)		(n=803)	(n=1,315)	
Abnormality	None	61.0%	65.2%	0.165	61.8%	62.5%	0.587
	Mild	31.4%	28.1%		31.1%	30.0%	
	Moderate	5.9%	6.0%		6.1%	5.9%	
	Severe	1.7%	0.8%		1.0%	1.7%	

[a] Analysis performed on natural logarithm of (1 – ratio of observed FEV_1 to observed FVC) scale; means transformed from natural logarithm of (1 – ratio of observed FEV_1 to observed FVC) scale; because of this transformation, a negative correlation implies a positive association between the ratio and the covariate.
--: Covariate not applicable for dependent variable.

Note: Correlations (r) are based on total sample size and are not category-specific.

APPENDIX G

List of Tables

APPENDIX G. SUMMARY OF ANALYSIS RESULTS

This appendix contains a summary of the results from the exposure analyses performed for this report and contained in Chapters 9 through 18. This summary is organized into 24 tables, grouped by analysis (unadjusted or adjusted), data form (continuous, dichotomous, or polytomous), and model (1, 2, 3, or 4). Each table contains a reference to its corresponding table in Chapters 9 through 18 and a description of the clinical parameter being summarized. The summary statistics, grouped by model and presented for each analysis and data form, are described below.

G.1 Model 1

For analyses of continuous data using Model 1 (Tables G-1 and G-13), the occupational category, Ranch Hand mean, Comparison mean, difference of Ranch Hand and Comparison means along with the associated 95-percent confidence interval (C.I.), and p-value are given for the unadjusted and adjusted analyses. For analyses of dichotomous data using Model 1 (Tables G-5 and G-17), the occupational category, estimated or adjusted relative risk and associated 95-percent confidence interval, and p-value are given for the unadjusted and adjusted analyses. The number and percentage of abnormalities within the Ranch Hand and Comparison groups are given for the unadjusted analyses. For analyses of polytomous data using Model 1 (Tables G-9 and G-21), the contrast (of the specified abnormal category versus the normal category), occupational category, estimated or adjusted relative risk and associated 95-percent confidence interval, and p-value are given for the unadjusted and adjusted analyses. The number and percentage of Ranch Hands and Comparisons within each abnormal level are given for the unadjusted analyses.

G.2 Models 2 and 4

For analyses of continuous data using Models 2 and 4, (Tables G-2 and G-14 for Model 2; Tables G-4 and G-16 for Model 4), the coefficient of determination (R^2), slope, standard error, and p-value are given for the unadjusted and adjusted analyses. For analyses of dichotomous data using Models 2 and 4 (Tables G-6 and G-18 for Model 2; Tables G-8 and G-20 for Model 4), the estimated or adjusted relative risk and associated 95-percent confidence interval, and p-value are given for the unadjusted and adjusted analyses. For analyses of polytomous data using Models 2 and 4 (Tables G-10 and G-22 for Model 2; Tables G-12 and G-24 for Model 4), the contrast (of the specified abnormal category versus the normal category), the estimated or adjusted relative risk and associated 95-percent confidence interval, and p-value are given for the unadjusted and adjusted analyses.

G.3 Model 3

For analyses of continuous data using Model 3 (Tables G-3 and G-17), the R^2, dioxin category, dioxin category sample size (n) and mean, difference of Ranch Hand dioxin category and Comparison dioxin category means along with the associated 95-percent confidence interval, and p-value are given for the unadjusted and adjusted analyses. For analyses of dichotomous data using Model 3 (Tables G-7 and G-19), the dioxin category, sample size, estimated or adjusted relative risk and associated 95-percent confidence interval for each Ranch Hand category versus Comparison contrast, and p-value are given for the unadjusted and adjusted analyses. The number and percentage of abnormalities within each dioxin category are given for unadjusted analyses. For analyses of polytomous data using Model 3 (Tables G-11

and G-23), the contrast (of the specified abnormal category versus the normal category), dioxin category, sample size, estimated or adjusted relative risk and associated 95-percent confidence interval for each Ranch Hand category versus Comparison contrast, and p-value are given for the unadjusted and adjusted analyses. The number and percentage of each abnormal level within each dioxin category are given for the unadjusted analyses.

A summary of the analysis (unadjusted or adjusted), data form (continuous, dichotomous, or polytomous), and model (1, 2, 3, or 4) for each table in Appendix G is given below.

Appendix G Table	Analysis	Data Form	Model
G-1	Unadjusted	Continuous	1
G-2	Unadjusted	Continuous	2
G-3	Unadjusted	Continuous	3
G-4	Unadjusted	Continuous	4
G-5	Unadjusted	Dichotomous	1
G-6	Unadjusted	Dichotomous	2
G-7	Unadjusted	Dichotomous	3
G-8	Unadjusted	Dichotomous	4
G-9	Unadjusted	Polytomous	1
G-10	Unadjusted	Polytomous	2
G-11	Unadjusted	Polytomous	3
G-12	Unadjusted	Polytomous	4
G-13	Adjusted	Continuous	1
G-14	Adjusted	Continuous	2
G-15	Adjusted	Continuous	3
G-16	Adjusted	Continuous	4
G-17	Adjusted	Dichotomous	1
G-18	Adjusted	Dichotomous	2
G-19	Adjusted	Dichotomous	3
G-20	Adjusted	Dichotomous	4
G-21	Adjusted	Polytomous	1
G-22	Adjusted	Polytomous	2
G-23	Adjusted	Polytomous	3
G-24	Adjusted	Polytomous	4

Table G-1. Summary of Unadjusted Results for Continuous Variables – Model 1 (Ranch Hands vs. Comparisons)

Table Ref.	Clinical Parameter (Units)	Occupational Category	Means RH	Means C	Difference of Means (95% C.I.)	p-Value
9-6	Body Fat (percent) [a]	All	22.09	22.28	–0.19 --	0.436
		Officer	22.04	21.87	0.17 --	0.656
		Enlisted Flyer	21.69	22.20	–0.51 --	0.390
		Enlisted Groundcrew	22.30	22.67	–0.37 --	0.318
9-8	Erythrocyte Sedimentation Rate (mm/hr) [b]	All	4.82	4.74	0.09 --	0.680
		Officer	4.36	4.41	–0.05 --	0.873
		Enlisted Flyer	5.35	5.83	–0.47 --	0.429
		Enlisted Groundcrew	5.06	4.71	0.35 --	0.263
10-35	PSA (ng/ml) [a]	All	1.104	1.120	–0.016 --	0.671
		Officer	1.195	1.229	–0.034 --	0.613
		Enlisted Flyer	1.241	1.234	0.007 --	0.949
		Enlisted Groundcrew	0.985	1.005	–0.020 --	0.693
13-11	AST (U/l) [a]	All	23.01	22.88	0.13 --	0.705
		Officer	23.40	23.34	0.06 --	0.914
		Enlisted Flyer	22.17	22.48	–0.32 --	0.696
		Enlisted Groundcrew	22.99	22.60	0.39 --	0.447
13-13	ALT (U/l) [a]	All	42.58	42.45	0.13 --	0.803
		Officer	42.21	41.79	0.42 --	0.613
		Enlisted Flyer	41.21	42.59	–1.38 --	0.290
		Enlisted Groundcrew	43.50	42.99	0.51 --	0.537
13-15	GGT (U/l) [a]	All	43.62	42.61	1.01 --	0.340
		Officer	42.32	40.74	1.57 --	0.332
		Enlisted Flyer	44.45	45.29	–0.84 --	0.758
		Enlisted Groundcrew	44.52	43.44	1.09 --	0.506
13-17	Alkaline Phosphatase (U/l) [a]	All	81.81	79.65	2.16 --	0.024
		Officer	78.44	76.74	1.70 --	0.241
		Enlisted Flyer	83.79	83.45	0.34 --	0.889
		Enlisted Groundcrew	84.22	81.04	3.18 --	0.030
13-19	Total Bilirubin (mg/dl) [a]	All	0.518	0.520	–0.002 --	0.857
		Officer	0.546	0.543	0.003 --	0.887
		Enlisted Flyer	0.489	0.513	–0.023 --	0.365
		Enlisted Groundcrew	0.506	0.503	0.003 --	0.869
13-22	Lactic Dehydrogenase (U/l) [a]	All	154.0	153.8	0.3 --	0.822
		Officer	153.9	154.4	–0.5 --	0.799
		Enlisted Flyer	152.3	152.5	–0.3 --	0.927
		Enlisted Groundcrew	154.9	153.7	1.2 --	0.488
13-24	Cholesterol (mg/dl) [c]	All	211.4	211.7	–0.3 --	0.838
		Officer	206.2	210.0	–3.8 --	0.149
		Enlisted Flyer	215.0	216.3	–1.3 --	0.760
		Enlisted Groundcrew	214.7	211.8	3.0 --	0.239

Table G-1. Summary of Unadjusted Results for Continuous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter (Units)	Occupational Category	Means RH	Means C	Difference of Means (95% C.I.)	p-Value
13-26	HDL Cholesterol (mg/dl) [a]	All	44.97	44.84	0.13 --	0.805
		Officer	46.64	46.68	–0.04 --	0.965
		Enlisted Flyer	45.07	43.58	1.49 --	0.240
		Enlisted Groundcrew	43.44	43.69	–0.25 --	0.739
13-28	Cholesterol-HDL Ratio [a]	All	4.66	4.68	–0.02 --	0.723
		Officer	4.39	4.46	–0.07 --	0.425
		Enlisted Flyer	4.72	4.93	–0.21 --	0.155
		Enlisted Groundcrew	4.90	4.81	0.10 --	0.282
13-30	Triglycerides (mg/dl) [a]	All	122.8	120.7	2.1 --	0.539
		Officer	114.9	111.7	3.2 --	0.523
		Enlisted Flyer	123.9	137.7	–13.8 --	0.122
		Enlisted Groundcrew	130.0	123.6	6.4 --	0.230
13-32	Creatine Phosphokinase (U/l) [a]	All	106.3	105.5	0.8 --	0.791
		Officer	105.8	104.3	1.4 --	0.748
		Enlisted Flyer	97.2	101.0	–3.8 --	0.562
		Enlisted Groundcrew	110.8	108.2	2.6 --	0.565
13-34	Serum Amylase (U/l) [a]	All	56.92	56.85	0.07 --	0.942
		Officer	54.88	57.86	–2.98 --	0.048
		Enlisted Flyer	58.46	55.91	2.55 --	0.284
		Enlisted Groundcrew	58.23	56.29	1.95 --	0.182
13-41	Prealbumin (mg/dl)	All	29.54	29.61	–0.07 (–0.50,0.37)	0.766
		Officer	29.65	29.87	–0.22 (–0.92,0.47)	0.532
		Enlisted Flyer	29.56	29.33	0.23 (–0.85,1.31)	0.679
		Enlisted Groundcrew	29.44	29.48	–0.03 (–0.70,0.63)	0.922
13-43	Albumin (mg/dl)	All	4,195.6	4,201.2	–5.6 (–34.9,23.8)	0.709
		Officer	4,172.9	4,204.6	–31.8 (–78.3,14.8)	0.181
		Enlisted Flyer	4,190.0	4,159.9	30.1 (–42.4,102.5)	0.416
		Enlisted Groundcrew	4,218.8	4,211.9	7.0 (–37.3,51.2)	0.758
13-45	α-1-Acid Glycoprotein (mg/dl) [a]	All	84.65	84.15	0.50 --	0.550
		Officer	80.89	82.22	–1.33 --	0.298
		Enlisted Flyer	85.49	85.88	–0.38 --	0.855
		Enlisted Groundcrew	87.92	85.31	2.61 --	0.044
13-47	α-1-Antitrypsin (mg/dl) [c]	All	150.0	146.5	3.5 --	0.002
		Officer	143.9	143.0	0.9 --	0.609
		Enlisted Flyer	155.3	151.1	4.2 --	0.136
		Enlisted Groundcrew	153.5	148.0	5.5 --	0.001
13-49	α-2-Macroglobulin (mg/dl) [a]	All	170.6	171.3	–0.7 --	0.726
		Officer	170.6	171.0	–0.4 --	0.901
		Enlisted Flyer	177.0	177.4	–0.4 --	0.935
		Enlisted Groundcrew	168.1	169.6	–1.5 --	0.608
13-51	Apolipoprotein B (mg/dl) [c]	All	110.5	111.5	–1.1 --	0.320
		Officer	106.4	109.6	–3.3 --	0.053
		Enlisted Flyer	113.2	115.2	–2.0 --	0.463
		Enlisted Groundcrew	113.1	112.0	1.2 --	0.479

Table G-1. Summary of Unadjusted Results for Continuous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter (Units)	Occupational Category	Means RH	Means C	Difference of Means (95% C.I.)	p-Value
13-53	C3 Complement (mg/dl) [a]	All	118.9	118.5	0.4 --	0.640
		Officer	114.9	114.6	0.3 --	0.814
		Enlisted Flyer	120.3	120.7	–0.4 --	0.862
		Enlisted Groundcrew	122.1	121.3	0.8 --	0.537
13-55	C4 Complement (mg/dl) [a]	All	25.71	25.91	–0.20 --	0.395
		Officer	24.73	25.54	–0.81 --	0.024
		Enlisted Flyer	26.52	25.50	–1.02 --	0.076
		Enlisted Groundcrew	26.31	26.38	–0.06 --	0.862
13-57	Haptoglobin (mg/dl) [c]	All	135.2	126.5	8.7 --	0.002
		Officer	122.4	116.3	6.1 --	0.140
		Enlisted Flyer	147.8	137.4	10.4 --	0.141
		Enlisted Groundcrew	142.5	132.3	10.2 --	0.016
13-59	Transferrin (mg/dl) [a]	All	252.7	249.6	3.1 --	0.044
		Officer	250.0	248.4	1.6 --	0.510
		Enlisted Flyer	254.5	251.5	3.0 --	0.439
		Enlisted Groundcrew	254.5	250.0	4.5 --	0.056
14-7	Systolic Blood Pressure (mm Hg) [a]	All	124.9	125.6	–0.7 --	0.383
		Officer	125.9	126.2	–0.2 --	0.865
		Enlisted Flyer	127.0	127.3	–0.3 --	0.875
		Enlisted Groundcrew	123.1	124.5	–1.4 --	0.241
14-9	Diastolic Blood Pressure (mm Hg) [c]	All	74.55	74.61	–0.06	0.883
		Officer	74.17	74.21	–0.04	0.952
		Enlisted Flyer	75.22	75.10	0.12	0.905
		Enlisted Groundcrew	74.63	74.80	–0.17	0.780
15-3	RBC Count (million/mm^3)	All	4.95	4.96	–0.02 (–0.05,0.02)	0.318
		Officer	4.89	4.92	–0.03 (–0.09,0.02)	0.234
		Enlisted Flyer	4.92	4.97	–0.04 (–0.12,0.04)	0.333
		Enlisted Groundcrew	5.01	5.00	0.01 (–0.04,0.06)	0.753
15-5	WBC Count (thousand/mm^3) [a]	All	6.67	6.65	0.02 --	0.789
		Officer	6.33	6.33	0.00 --	0.970
		Enlisted Flyer	6.72	6.86	–0.14 --	0.474
		Enlisted Groundcrew	6.97	6.86	0.11 --	0.358
15-7	Hemoglobin (gm/dl)	All	15.32	15.33	0.00 (–0.09,0.09)	0.979
		Officer	15.23	15.29	–0.06 (–0.20,0.08)	0.389
		Enlisted Flyer	15.29	15.38	–0.08 (–0.30,0.13)	0.445
		Enlisted Groundcrew	15.42	15.34	0.09 (–0.05,0.22)	0.206
15-9	Hematocrit (percent)	All	45.56	45.59	–0.04 (–0.31,0.24)	0.798
		Officer	45.24	45.48	–0.24 (–0.67,0.19)	0.274
		Enlisted Flyer	45.49	45.72	–0.23 (–0.90,0.44)	0.504
		Enlisted Groundcrew	45.88	45.65	0.22 (–0.18,0.63)	0.279
15-11	Platelet Count (thousand/mm^3) [c]	All	207.0	203.9	3.1 --	0.150
		Officer	196.6	205.1	–8.5 --	0.012
		Enlisted Flyer	213.8	198.8	14.9 --	0.005
		Enlisted Groundcrew	213.9	204.6	9.3 --	0.004

Table G-1. Summary of Unadjusted Results for Continuous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter (Units)	Occupational Category	Means RH	Means C	Difference of Means (95% C.I.)	p-Value
15-13	Prothrombin Time (seconds) [a]	All	10.48	10.49	–0.01 --	0.870
		Officer	10.54	10.52	0.02 --	0.720
		Enlisted Flyer	10.46	10.49	–0.03 --	0.748
		Enlisted Groundcrew	10.45	10.47	–0.02 --	0.714
15-16	Absolute Neutrophils (segs) (thousand/mm^3) [a]	All	3.84	3.81	0.03 --	0.612
		Officer	3.59	3.61	–0.02 --	0.804
		Enlisted Flyer	3.92	3.95	–0.02 --	0.885
		Enlisted Groundcrew	4.06	3.95	–0.01 --	0.263
15-17	Absolute Neutrophils (bands) (Nonzero Measurements) (thousand/mm^3) [a]	All	0.201	0.189	0.012 --	0.123
		Officer	0.194	0.180	0.014 --	0.250
		Enlisted Flyer	0.190	0.204	–0.014 --	0.478
		Enlisted Groundcrew	0.213	0.193	0.021 --	0.089
15-19	Absolute Lymphocytes (thousand/mm^3) [a]	All	1.76	1.75	0.00 --	0.920
		Officer	1.70	1.67	0.04 --	0.392
		Enlisted Flyer	1.71	1.79	–0.08 --	0.248
		Enlisted Groundcrew	1.83	1.82	0.01 --	0.891
15-20	Absolute Monocytes (thousands/mm^3) [c]	All	0.477	0.481	–0.004 --	0.648
		Officer	0.463	0.471	–0.008 --	0.594
		Enlisted Flyer	0.470	0.507	–0.037 --	0.118
		Enlisted Groundcrew	0.492	0.482	0.011 --	0.455
15-21	Absolute Eosinophils (Nonzero Measurements) (thousand/mm^3) [a]	All	0.159	0.161	–0.002 --	0.684
		Officer	0.160	0.153	0.007 --	0.422
		Enlisted Flyer	0.162	0.164	–0.002 --	0.895
		Enlisted Groundcrew	0.157	0.167	–0.011 --	0.183
15-23	Absolute Basophils (Nonzero Measurements) (thousand/mm^3) [a]	All	0.078	0.080	–0.002 --	0.315
		Officer	0.076	0.077	–0.001 --	0.838
		Enlisted Flyer	0.079	0.082	–0.003 --	0.577
		Enlisted Groundcrew	0.079	0.082	–0.003 --	0.322
16-6	Time to Diabetes Onset (years)	All	--	--	--	0.603
		Officer	--	--	--	0.916
		Enlisted Flyer	--	--	--	0.740
		Enlisted Groundcrew	--	--	--	0.715
16-9	TSH (μIU/ml) [a]	All	1.88	1.81	–0.08 --	0.130
		Officer	2.01	1.89	0.12 --	0.170
		Enlisted Flyer	1.72	1.82	–0.10 --	0.428
		Enlisted Groundcrew	1.84	1.73	0.11 --	0.139
16-11	Thyroxine (μg/dl) [c]	All	7.07	7.04	0.03 --	0.601
		Officer	6.76	6.84	–0.08 --	0.373
		Enlisted Flyer	7.28	7.24	0.03 --	0.818
		Enlisted Groundcrew	7.27	7.15	0.12 --	0.154
16-14	Fasting Glucose (mg/dl) [a]	All	101.4	101.8	–0.3 --	0.745
		Officer	101.0	100.0	1.1 --	0.468
		Enlisted Flyer	103.2	104.9	–1.7 --	0.507
		Enlisted Groundcrew	101.0	102.3	–1.3 --	0.388

Table G-1. Summary of Unadjusted Results for Continuous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter (Units)	Occupational Category	Means RH	Means C	Difference of Means (95% C.I.)	p-Value
16-16	2-Hour Postprandial Glucose (mg/dl) [a]	All	105.2	104.9	0.3 --	0.818
		Officer	106.1	101.8	4.3 --	0.053
		Enlisted Flyer	107.8	111.3	–3.5 --	0.342
		Enlisted Groundcrew	103.4	105.8	–2.3 --	0.274
16-20	Serum Insulin (μIU/ml) [a]	All	47.95	47.92	0.03 --	0.990
		Officer	45.60	42.40	3.20 --	0.283
		Enlisted Flyer	49.81	54.92	–5.11 --	0.369
		Enlisted Groundcrew	49.49	51.33	–1.84 --	0.574
16-22	α-1-C Hemoglobin (percent) [a]	All	6.48	6.49	–0.01 --	0.919
		Officer	6.37	6.31	0.07 --	0.387
		Enlisted Flyer	6.53	6.67	–0.14 --	0.280
		Enlisted Groundcrew	6.57	6.59	–0.03 --	0.714
16-24	Total Testosterone (ng/dl) [c]	All	423.1	422.6	0.5 --	0.945
		Officer	406.9	413.4	–6.4 --	0.606
		Enlisted Flyer	439.6	428.4	11.2 --	0.577
		Enlisted Groundcrew	431.2	428.7	2.5 --	0.835
16-26	Free Testosterone (pg/ml) [c]	All	13.96	13.92	0.04 --	0.852
		Officer	12.91	13.26	–0.36 --	0.269
		Enlisted Flyer	14.03	13.95	0.08 --	0.878
		Enlisted Groundcrew	14.89	14.49	0.40 --	0.209
16-28	Estradiol (pg/ml) [c]	All	40.06	40.63	–0.57 --	0.434
		Officer	38.38	41.81	–3.43 --	0.003
		Enlisted Flyer	42.87	40.70	2.17 --	0.238
		Enlisted Groundcrew	40.49	39.60	0.89 --	0.418
16-30	LH (mIU/ml) [a]	All	3.86	3.86	0.00 --	0.979
		Officer	4.09	3.82	0.27 --	0.131
		Enlisted Flyer	3.67	4.02	–0.34 --	0.194
		Enlisted Groundcrew	3.74	3.85	–0.11 --	0.491
16-32	FSH (mIU/ml) [a]	All	6.05	5.98	0.07 --	0.666
		Officer	6.62	6.11	0.51 --	0.071
		Enlisted Flyer	6.02	5.99	0.03 --	0.941
		Enlisted Groundcrew	5.59	5.86	–0.27 --	0.257
17-4	CD3+ Cells (T Cells) (cells/mm^3) [a]	All	1,231.0	1,257.7	–26.7 --	0.431
		Officer	1,230.0	1,190.2	39.8 --	0.449
		Enlisted Flyer	1,197.2	1,286.8	–89.6 --	0.270
		Enlisted Groundcrew	1,247.1	1,301.3	–54.2 --	0.308
17-5	CD4+ Cells (Helper T Cells) (cells/mm^3) [a]	All	842.0	857.0	–15.0 --	0.511
		Officer	838.0	824.7	13.3 --	0.708
		Enlisted Flyer	808.4	870.2	–61.8 --	0.254
		Enlisted Groundcrew	861.4	877.9	–16.5 --	0.646
17-6	CD8+ Cells (Suppressor T Cells) (cells/mm^3) [a]	All	564.5	587.1	–22.6 --	0.254
		Officer	558.7	551.7	7.0 --	0.818
		Enlisted Flyer	563.9	625.6	–61.7 --	0.207
		Enlisted Groundcrew	571.0	601.7	–30.7 --	0.319

Table G-1. Summary of Unadjusted Results for Continuous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter (Units)	Occupational Category	Means RH	Means C	Difference of Means (95% C.I.)	p-Value
17-7	CD16+56+ Cells (Natural Killer Cells) ($cells/mm^3$) [a]	All	259.3	275.9	−16.6 --	0.082
		Officer	266.2	276.1	−9.9 --	0.521
		Enlisted Flyer	236.7	290.2	−53.5 --	0.018
		Enlisted Groundcrew	262.4	270.6	−8.2 --	0.572
17-8	CD20+ Cells (B Cells) ($cells/mm^3$) [a]	All	184.0	185.5	−1.5 --	0.858
		Officer	175.3	167.1	8.1 --	0.496
		Enlisted Flyer	170.2	185.2	−15.0 --	0.420
		Enlisted Groundcrew	200.4	201.1	−0.7 --	0.961
17-9	CD3+CD4+ Cells (Helper T Cells) ($cells/mm^3$) [a]	All	767.4	780.9	−13.4 --	0.541
		Officer	763.1	749.6	13.5 --	0.693
		Enlisted Flyer	737.4	791.9	−54.5 --	0.296
		Enlisted Groundcrew	785.6	801.8	−16.1 --	0.641
17-10	Absolute Lymphocytes ($cells/mm^3$) [a]	All	1,781.2	1,777.9	3.2 --	0.909
		Officer	1,730.0	1,685.2	44.8 --	0.292
		Enlisted Flyer	1,753.3	1,817.2	−63.8 --	0.360
		Enlisted Groundcrew	1,840.2	1,849.6	−9.5 --	0.828
17-11	IgA (mg/dl) [a]	All	232.4	233.3	−0.9 --	0.860
		Officer	224.8	225.2	−0.4 --	0.958
		Enlisted Flyer	238.1	236.6	1.4 --	0.912
		Enlisted Groundcrew	237.3	239.5	−2.2 --	0.779
17-12	IgG (mg/dl) [a]	All	1,035.5	1,047.3	−11.8 --	0.273
		Officer	1,022.2	1,029.8	−7.7 --	0.649
		Enlisted Flyer	1,021.8	1,048.9	−27.2 --	0.307
		Enlisted Groundcrew	1,053.3	1,062.2	−8.9 --	0.587
17-13	IgM (mg/dl) [a]	All	96.3	98.4	−2.1 --	0.373
		Officer	95.2	95.9	−0.6 --	0.862
		Enlisted Flyer	94.6	104.4	−9.7 --	0.102
		Enlisted Groundcrew	98.0	98.7	−0.8 --	0.831
18-8	FVC (percent of predicted)	All	99.31	98.93	0.38 (−0.91,1.68)	0.564
		Officer	100.48	100.14	0.33 (−1.73,2.39)	0.753
		Enlisted Flyer	99.64	98.88	0.75 (−2.45,3.96)	0.645
		Enlisted Groundcrew	98.14	97.90	0.24 (−1.71,2.18)	0.811
18-9	FEV_1 (percent of predicted)	All	94.13	94.28	−0.15 (−1.66,1.37)	0.849
		Officer	95.47	95.65	−0.18 (−2.58,2.23)	0.886
		Enlisted Flyer	91.09	92.30	−1.21 (−4.95,2.54)	0.527
		Enlisted Groundcrew	94.14	93.74	0.40 (−1.87,2.67)	0.729
18-10	Ratio of Observed FEV_1 to Observed FVC [d]	All	0.760	0.763	−0.003 --	0.366
		Officer	0.756	0.761	−0.005 --	0.376
		Enlisted Flyer	0.741	0.748	−0.007 --	0.431
		Enlisted Groundcrew	0.772	0.771	0.001 --	0.843

[a] Means transformed from natural logarithm scale; difference of means after transformation to original scale; confidence interval not given because analysis was performed on natural logarithm scale; p-value based on difference of means on natural logarithm scale.

Table G-1. Summary of Unadjusted Results for Continuous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

[b] Means transformed from natural logarithm (clinical parameter + 0.1) scale; difference of means after transformation to original scale; confidence interval not given because analysis was performed on natural logarithm (clinical parameter + 0.1) scale; p-value based on difference of means on natural logarithm (clinical parameter + 0.1) scale.
[c] Means transformed from square root scale; difference of means after transformation to original scale; confidence interval not given because analysis was performed on square root scale; p-value based on difference of means on square root scale.
[d] Means transformed from natural logarithm (1 – clinical parameter) scale; difference of means after transformation to original scale; confidence interval not given because analysis was performed on natural logarithm (1 – clinical parameter) scale; p-value based on difference of means on natural logarithm (1 – clinical parameter) scale.

Note: RH = Ranch Hand; C = Comparison.

Table G-2. Summary of Unadjusted Results for Continuous Variables – Model 2 (Ranch Hands: Log_2 (Initial Dioxin))

Table Ref.	Clinical Parameter (Units)	R^2	Slope (Standard Error)[a]	p-Value
9-6	Body Fat (percent)[b]	0.006	0.015 (0.009)	0.081
9-8	Erythrocyte Sedimentation Rate (mm/hr)[c]	0.009	0.029 (0.034)	0.387
10-35	PSA (ng/ml)[b]	0.037	–0.071 (0.027)	0.010
13-11	AST (U/l)[b]	0.011	0.003 (0.012)	0.813
13-13	ALT (U/l)[b]	0.036	0.013 (0.010)	0.199
13-15	GGT (U/l)[b]	0.013	0.004 (0.019)	0.823
13-17	Alkaline Phosphatase (U/l)[b]	0.009	–0.004 (0.009)	0.646
13-19	Total Bilirubin (mg/dl)[b]	0.013	–0.014 (0.016)	0.368
13-22	Lactic Dehydrogenase (U/l)[b]	0.009	–0.001 (0.006)	0.908
13-24	Cholesterol (mg/dl)[d]	0.017	0.129 (0.046)	0.005
13-26	HDL Cholesterol (mg/dl)[b]	0.053	–0.009 (0.009)	0.312
13-28	Cholesterol-HDL Ratio[b]	0.055	0.028 (0.009)	0.003
13-30	Triglycerides (mg/dl)[b]	0.025	0.033 (0.023)	0.140
13-32	Creatine Phosphokinase (U/l)[b]	0.013	0.005 (0.021)	0.800
13-34	Serum Amylase (U/l)[b]	0.052	–0.024 (0.013)	0.070
13-41	Prealbumin (mg/dl)	0.030	–0.041 (0.178)	0.818
13-43	Albumin (mg/dl)	0.023	13.830 (10.970)	0.208
13-45	α-1-Acid Glycoprotein (mg/dl)[b]	<0.001	0.000 (0.008)	0.992
13-47	α-1-Antitrypsin (mg/dl)[d]	0.013	0.066 (0.036)	0.071
13-49	α-2-Macroglobulin (mg/dl)[b]	<0.001	–0.004 (0.009)	0.698
13-51	Apolipoprotein B (mg/dl)[d]	0.014	0.107 (0.041)	0.009
13-53	C3 Complement (mg/dl)[b]	0.071	0.012 (0.005)	0.023
13-55	C4 Complement (mg/dl)[b]	0.002	–0.003 (0.007)	0.701
13-57	Haptoglobin (mg/dl)[d]	0.002	0.084 (0.097)	0.387
13-59	Transferrin (mg/dl)[b]	0.001	0.003 (0.005)	0.594
14-7	Systolic Blood Pressure (mm Hg)[b]	0.049	–0.006 (0.005)	0.238
14-9	Diastolic Blood Pressure (mm Hg)[d]	0.023	0.025 (0.019)	0.190
15-3	RBC Count (million/mm^3)	0.019	0.023 (0.014)	0.102
15-5	WBC Count (thousand/mm^3)[b]	0.022	0.019 (0.009)	0.035
15-7	Hemoglobin (gm/dl)	0.011	0.078 (0.034)	0.023
15-9	Hematocrit (percent)	0.011	0.241 (0.104)	0.021
15-11	Platelet Count (thousand/mm^3)[d]	0.016	0.145 (0.057)	0.012
15-13	Prothrombin Time (seconds)[b]	0.004	–0.001 (0.003)	0.572
15-16	Absolute Neutrophils (segs) (thousand/mm^3)[b]	0.015	0.019 (0.012)	0.115
15-17	Absolute Neutrophils (Nonzero Measurements) (bands) (thousand/mm^3)[b]	0.004	–0.031 (0.032)	0.343
15-19	Absolute Lymphocytes (thousand/mm^3)[b]	0.021	0.023 (0.012)	0.063
15-20	Absolute Monocytes (thousand/mm^3)[d]	0.003	0.003 (0.006)	0.568
15-21	Absolute Eosinophils (Nonzero Measurements) (thousand/mm^3)[b]	0.001	0.005 (0.025)	0.836
15-23	Absolute Basophils (Nonzero Measurements) (thousand/mm^3)[b]	0.013	0.009 (0.022)	0.685
16-6	Time to Diabetes Onset (years)[e]	--	–0.021 (0.023)	0.356
16-9	TSH (μIU/ml)[b]	0.002	–0.015 (0.021)	0.475
16-11	Thyroxine (μg/dl)[d]	0.012	0.010 (0.008)	0.250
16-14	Fasting Glucose (mg/dl)[b]	0.102	0.011 (0.008)	0.174

Table G-2. Summary of Unadjusted Results for Continuous Variables – Model 2 (Ranch Hands: Log_2 (Initial Dioxin)) (Continued)

Table Ref.	Clinical Parameter (Units)	R^2	Slope (Standard Error)[a]	p-Value
16-16	2-Hour Postprandial Glucose (mg/dl) [b]	0.076	–0.010 (0.011)	0.363
16-20	Serum Insulin (μIU/ml) [b]	0.092	0.020 (0.036)	0.571
16-22	α-1-C Hemoglobin (percent) [b]	0.107	0.017 (0.006)	0.009
16-24	Total Testosterone (ng/dl) [d]	0.118	0.287 (0.144)	0.047
16-26	Free Testosterone (pg/ml) [d]	0.084	0.066 (0.022)	0.003
16-28	Estradiol (pg/ml) [d]	0.007	0.084 (0.049)	0.087
16-30	LH (mIU/ml) [b]	0.001	–0.016 (0.023)	0.496
16-32	FSH (mIU/ml) [b]	0.008	–0.035 (0.021)	0.099
17-4	CD3+ Cells (T Cells) (cells/mm^3) [b]	0.013	0.023 (0.023)	0.317
17-5	CD4+ Cells (Helper T Cells) (cells/mm^3) [b]	0.018	0.027 (0.023)	0.254
17-6	CD8+ Cells (Suppressor T Cells) (cells/mm^3) [b]	0.001	0.012 (0.029)	0.688
17-7	CD16+56+ Cells (Natural Killer Cells) (cells/mm^3) [b]	0.038	–0.029 (0.032)	0.370
17-8	CD20+ Cells (B Cells) (cells/mm^3) [b]	0.052	0.081 (0.035)	0.024
17-9	CD3+CD4+ Cells (Helper T Cells) (cells/mm^3) [b]	0.018	0.030 (0.024)	0.226
17-10	Absolute Lymphocytes (cells/mm^3) [b]	0.019	0.019 (0.012)	0.121
17-11	IgA (mg/dl) [b]	0.007	0.021 (0.017)	0.224
17-12	IgG (mg/dl) [b]	0.002	–0.001 (0.009)	0.922
17-13	IgM (mg/dl) [b]	0.005	0.007 (0.019)	0.711
18-8	FVC (percent of predicted)	0.018	0.332 (0.491)	0.499
18-9	FEV_1 (percent of predicted)	0.006	0.870 (0.581)	0.135
18-10	Observed FEV_1 to Observed FVC [f]	0.053	–0.026 (0.011)	0.023

[a] Adjusted for percent body fat at the time of the blood measurement for dioxin.
[b] Slope and standard error based on natural logarithm of clinical parameter versus log_2 (initial dioxin).
[c] Slope and standard error based on natural logarithm of (clinical parameter + 0.1) versus log_2 (initial dioxin).
[d] Slope and standard error based on square root of clinical parameter versus log_2 (initial dioxin).
[e] Slope and standard error based on time to diabetes onset versus log_2 (initial dioxin) under a censored Weibull distribution.
[f] Slope and standard error based on natural logarithm of (1 – clinical parameter) versus log_2 (initial dioxin).
--: R-squared not presented because analysis was based on a censored Weibull distribution.

Table G-3. Summary of Unadjusted Results for Continuous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category)

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Adj. Mean[a]	Difference of Means vs. Comparisons (95% C.I.)	p-Value
9-6	Body Fat (percent)[b]	0.025	Comparison	1,213	22.26		
			Background RH	381	20.64	–1.62 --	<0.001
			Low RH	239	23.04	0.78 --	0.045
			High RH	243	23.57	1.31 --	0.001
			Low plus High RH	482	23.30	1.04 --	0.001
9-8	Erythrocyte Sedimentation Rate (mm/hr)[c]	0.022	Comparison	1,213	4.74		
			Background RH	381	4.48	–0.26 --	0.323
			Low RH	239	5.06	0.32 --	0.350
			High RH	243	5.12	0.38 --	0.259
			Low plus High RH	482	5.09	0.35 --	0.176
10-35	PSA (ng/ml)[b]	0.009	Comparison	1,152	1.127		
			Background RH	365	1.099	–0.028 --	0.587
			Low RH	222	1.205	0.078 --	0.227
			High RH	236	1.023	–0.104 --	0.079
			Low plus High RH	458	1.108	–0.019 --	0.692
13-11	AST (U/l)[b]	0.011	Comparison	1,194	22.84		
			Background RH	376	22.54	–0.30 --	0.501
			Low RH	236	23.39	0.55 --	0.306
			High RH	240	23.36	0.52 --	0.334
			Low plus High RH	476	23.37	0.53 --	0.193
13-13	ALT (U/l)[b]	0.039	Comparison	1,194	42.37		
			Background RH	376	41.32	–1.05 --	0.129
			Low RH	236	43.14	0.77 --	0.368
			High RH	240	44.27	1.90 --	0.027
			Low plus High RH	476	43.71	1.34 --	0.041

Table G-3. Summary of Unadjusted Results for Continuous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Adj. Mean[a]	Difference of Means vs. Comparisons (95% C.I.)	p-Value
13-15	GGT (U/l)[b]	0.026	Comparison	1,194	42.21		
			Background RH	376	40.81	–1.40 --	0.296
			Low RH	236	43.99	1.78 --	0.283
			High RH	240	47.38	5.17 --	0.003
			Low plus High RH	476	45.67	3.46 --	0.007
13-17	Alkaline Phosphatase (U/l)[b]	0.003	Comparison	1,194	79.57		
			Background RH	376	81.50	1.93 --	0.130
			Low RH	236	82.34	2.78 --	0.070
			High RH	240	81.36	1.79 --	0.238
			Low plus High RH	476	81.85	2.28 --	0.051
13-19	Total Bilirubin (mg/dl)[b]	0.002	Comparison	1,194	0.520		
			Background RH	376	0.526	0.006 --	0.673
			Low RH	236	0.516	–0.004 --	0.828
			High RH	240	0.506	–0.014 --	0.418
			Low plus High RH	476	0.511	–0.009 --	0.500
13-22	Lactic Dehydrogenase (U/l)[b]	0.027	Comparison	1,192	153.7		
			Background RH	376	154.3	0.6 --	0.693
			Low RH	236	153.6	–0.1 --	0.941
			High RH	240	154.1	0.4 --	0.816
			Low plus High RH	476	153.8	0.1 --	0.916
13-24	Cholesterol (mg/dl)[d]	0.006	Comparison	1,194	211.7		
			Background RH	376	208.8	–2.9 --	0.183
			Low RH	236	209.3	–2.4 --	0.351
			High RH	240	217.4	5.7 --	0.032
			Low plus High RH	476	213.4	1.7 --	0.422
13-26	HDL Cholesterol (mg/dl)[b]	0.059	Comparison	1,193	44.79		
			Background RH	376	45.54	0.75 --	0.269
			Low RH	235	45.23	0.44 --	0.585
			High RH	240	43.58	–1.21 --	0.130
			Low plus High RH	475	44.39	–0.40 --	0.519

Table G-3. Summary of Unadjusted Results for Continuous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Adj. Mean[a]	Difference of Means vs. Comparisons (95% C.I.)	p-Value
13-28	Cholesterol-HDL Ratio[b]	0.046	Comparison	1,193	4.69		
			Background RH	376	4.55	–0.14 --	0.068
			Low RH	235	4.58	–0.11 --	0.220
			High RH	240	4.95	0.26 --	0.005
			Low plus High RH	475	4.76	0.07 --	0.282
13-30	Triglycerides (mg/dl)[b]	0.057	Comparison	1,194	120.3		
			Background RH	375	114.5	–5.8 --	0.172
			Low RH	236	119.7	–0.6 --	0.897
			High RH	240	140.4	20.1 --	<0.001
			Low plus High RH	476	129.7	9.4 --	0.023
13-32	Creatine Phosphokinase (U/l)[b]	0.026	Comparison	1,194	105.4		
			Background RH	376	105.6	0.2 --	0.961
			Low RH	236	108.2	2.8 --	0.547
			High RH	240	106.3	0.9 --	0.843
			Low plus High RH	476	107.2	1.8 --	0.602
13-34	Serum Amylase (U/l)[b]	0.039	Comparison	1,194	56.88		
			Background RH	376	55.87	–1.01 --	0.419
			Low RH	236	60.54	3.66 --	0.019
			High RH	240	54.89	–1.99 --	0.178
			Low plus High RH	476	57.63	0.75 --	0.523
13-41	Prealbumin (mg/dl)	0.017	Comparison	1,194	29.62		
			Background RH	376	29.53	–0.09 (–0.67,0.49)	0.760
			Low RH	236	29.47	–0.15 (–0.85,0.54)	0.665
			High RH	240	29.65	0.03 (–0.66,0.73)	0.927
			Low plus High RH	476	29.56	–0.06 (–0.59,0.47)	0.825
13-43	Albumin (mg/dl)	0.017	Comparison	1,194	4,199.7		
			Background RH	376	4,200.6	0.9 (–37.7,39.6)	0.962
			Low RH	236	4,155.3	–44.5 (–90.8,1.8)	0.060
			High RH	240	4,228.9	29.2 (–16.9,75.3)	0.215
			Low plus High RH	476	4,192.4	–7.3 (–42.6,28.0)	0.685

Table G-3. *Summary of Unadjusted Results for Continuous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)*

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Adj. Mean[a]	Difference of Means vs. Comparisons (95% C.I.)	p-Value
13-45	α-1-Acid Glycoprotein (mg/dl)[b]	0.003	Comparison	1,194	84.29		
			Background RH	376	83.02	–1.27 --	0.256
			Low RH	236	84.82	0.53 --	0.692
			High RH	240	87.02	2.73 --	0.045
			Low plus High RH	476	85.92	1.63 --	0.114
13-47	α-1-Antitrypsin (mg/dl)[d]	0.008	Comparison	1,194	146.8		
			Background RH	376	147.9	1.1 --	0.470
			Low RH	236	148.9	2.1 --	0.244
			High RH	240	154.0	7.2 --	<0.001
			Low plus High RH	476	151.4	4.6 --	0.001
13-49	α-2-Macroglobulin (mg/dl)[b]	0.001	Comparison	1,194	171.2		
			Background RH	376	170.2	–1.0 --	0.706
			Low RH	236	170.2	–1.0 --	0.747
			High RH	240	170.2	–1.0 --	0.741
			Low plus High RH	476	170.2	–1.0 --	0.669
13-51	Apolipoprotein B (mg/dl)[d]	0.005	Comparison	1,194	111.5		
			Background RH	376	108.8	–2.7 --	0.057
			Low RH	236	108.9	–2.6 --	0.131
			High RH	240	114.6	3.1 --	0.073
			Low plus High RH	476	111.8	0.3 --	0.843
13-53	C3 Complement (mg/dl)[b]	0.096	Comparison	1,194	118.5		
			Background RH	376	116.7	–1.8 --	0.107
			Low RH	236	119.5	1.0 --	0.399
			High RH	240	122.3	3.8 --	0.003
			Low plus High RH	476	120.9	2.4 --	0.013
13-55	C4 Complement (mg/dl)[b]	0.012	Comparison	1,194	25.90		
			Background RH	376	25.41	–0.49 --	0.109
			Low RH	236	26.03	0.13 --	0.733
			High RH	240	25.91	0.01 --	0.986
			Low plus High RH	476	25.97	0.07 --	0.816

Table G-3. Summary of Unadjusted Results for Continuous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Adj. Mean[a]	Difference of Means vs. Comparisons (95% C.I.)	p-Value
13-57	Haptoglobin (mg/dl)[d]	0.006	Comparison	1,194	126.7		
			Background RH	376	131.4	4.7 --	0.210
			Low RH	236	134.5	7.8 --	0.078
			High RH	240	141.7	15.0 --	0.001
			Low plus High RH	476	138.1	11.4 --	0.001
13-59	Transferrin (mg/dl)[b]	0.004	Comparison	1,194	249.5		
			Background RH	376	250.9	1.4 --	0.480
			Low RH	236	251.9	2.4 --	0.328
			High RH	240	255.9	6.4 --	0.010
			Low plus High RH	476	253.9	4.4 --	0.019
14-7	Systolic Blood Pressure (mm Hg)[b]	0.040	Comparison	1,195	125.5		
			Background RH	376	125.4	–0.1 --	0.935
			Low RH	233	125.9	0.4 --	0.730
			High RH	243	123.4	–2.1 --	0.079
			Low plus High RH	476	124.6	–0.9 --	0.346
14-9	Diastolic Blood Pressure (mm Hg)[d]	0.014	Comparison	1,195	74.57		
			Background RH	376	74.14	–0.43 --	0.432
			Low RH	233	74.19	–0.38 --	0.569
			High RH	243	75.65	1.08 --	0.099
			Low plus High RH	476	74.93	0.36 --	0.468
15-3	RBC Count (million/mm^3)	0.011	Comparison	1,211	4.96		
			Background RH	381	4.95	–0.01 (–0.06,0.03)	0.540
			Low RH	239	4.92	–0.05 (–0.01,0.01)	0.094
			High RH	239	4.98	0.02 (–0.04,0.07)	0.506
			Low plus High RH	478	4.95	–0.01 (–0.05,0.03)	0.510
15-5	WBC Count (thousand/mm^3)[b]	0.010	Comparison	1,211	6.64		
			Background RH	381	6.57	–0.07 --	0.493
			Low RH	239	6.56	–0.08 --	0.491
			High RH	239	6.92	0.28 --	0.029
			Low plus High RH	478	6.73	0.09 --	0.324

Table G-3. Summary of Unadjusted Results for Continuous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Adj. Mean[a]	Difference of Means vs. Comparisons (95% C.I.)	p-Value
15-7	Hemoglobin (gm/dl)	0.002	Comparison	1,211	15.33		
			Background RH	381	15.30	–0.03 (–0.14.0.09)	0.641
			Low RH	239	15.26	–0.07 (–0.21,0.07)	0.319
			High RH	239	15.46	0.12 (–0.01,0.26)	0.080
			Low plus High RH	478	15.36	0.03 (–0.08,0.13)	0.617
15-9	Hematocrit (percent)	0.003	Comparison	1,211	45.61		
			Background RH	381	45.56	–0.06 (–0.41,0.30)	0.756
			Low RH	239	45.30	–0.31 (–0.74,0.12)	0.153
			High RH	239	45.93	0.32 (–0.11,0.75)	0.147
			Low plus High RH	478	45.61	0.00 (–0.32,0.33)	0.987
15-11	Platelet Count (thousand/mm^3)[d]	0.016	Comparison	1,205	204.6		
			Background RH	379	202.1	–2.5 --	0.374
			Low RH	238	204.6	–0.1 --	0.987
			High RH	238	217.2	12.6 --	<0.001
			Low plus High RH	476	210.8	6.2 --	0.017
15-13	Prothrombin Time (seconds)[b]	0.002	Comparison	987	10.49		
			Background RH	309	10.53	0.04 --	0.476
			Low RH	182	10.46	–0.03 --	0.667
			High RH	193	10.44	–0.05 --	0.411
			Low plus High RH	375	10.45	–0.04 --	0.409
15-16	Absolute Neutrophils (segs) (thousand/mm^3)[b]	0.007	Comparison	1,211	3.81		
			Background RH	381	3.75	–0.06 --	0.430
			Low RH	239	3.80	–0.01 --	0.906
			High RH	239	4.03	0.22 --	0.028
			Low plus High RH	478	3.91	0.10 --	0.172
15-17	Absolute Neutrophils (bands) (Nonzero Measurements) (thousand/mm^3)[b]	0.005	Comparison	1,002	0.189		
			Background RH	316	0.191	0.002 --	0.783
			Low RH	196	0.211	0.022 --	0.079
			High RH	201	0.209	0.020 --	0.113
			Low plus High RH	397	0.210	0.021 --	0.029

Table G-3. *Summary of Unadjusted Results for Continuous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)*

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Adj. Mean[a]	Difference of Means vs. Comparisons (95% C.I.)	p-Value
15-19	Absolute Lymphocytes (thousand/mm^3)[b]	0.005	Comparison	1,211	1.75		
			Background RH	381	1.77	0.02 --	0.671
			Low RH	239	1.71	–0.04 --	0.383
			High RH	239	1.78	0.03 --	0.575
			Low plus High RH	478	1.74	–0.01 --	0.839
15-20	Absolute Monocytes (thousand/mm^3)[d]	0.011	Comparison	1,211	0.480		
			Background RH	381	0.464	–0.016 --	0.221
			Low RH	239	0.469	–0.011 --	0.480
			High RH	239	0.502	0.022 --	0.136
			Low plus High RH	478	0.486	0.006 --	0.606
15-21	Absolute Eosinophils (Nonzero Measurements) (thousand/mm^3)[b]	0.001	Comparison	1,064	0.161		
			Background RH	337	0.163	0.002 --	0.805
			Low RH	206	0.155	–0.006 --	0.513
			High RH	211	0.154	–0.007 --	0.434
			Low plus High RH	417	0.155	–0.006 --	0.346
15-23	Absolute Basophils (Nonzero Measurements) (thousand/mm^3)[b]	0.003	Comparison	562	0.080		
			Background RH	168	0.078	–0.002 --	0.410
			Low RH	92	0.076	–0.004 --	0.222
			High RH	109	0.080	0.000 --	0.930
			Low plus High RH	201	0.078	–0.002 --	0.482
16-6	Time to Diabetes Onset (years)	--	Comparison	1,195	--		
			Background RH	379	--	--	0.013
			Low RH	235	--	--	0.254
			High RH	240	--	--	0.233
			Low plus High RH	475	--	--	0.134
16-9	TSH (μIU/ml)[b]	0.002	Comparison	1,161	1.80		
			Background RH	367	1.91	0.11 --	0.129
			Low RH	233	1.89	0.09 --	0.273
			High RH	234	1.81	0.01 --	0.942
			Low plus High RH	467	1.85	0.05 --	0.446

Table G-3. Summary of Unadjusted Results for Continuous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Adj. Mean[a]	Difference of Means vs. Comparisons (95% C.I.)	p-Value
16-11	Thyroxine (μg/dl)[d]	0.004	Comparison	1,161	7.04		
			Background RH	367	6.95	–0.09 --	0.221
			Low RH	233	7.13	0.09 --	0.344
			High RH	234	7.23	0.19 --	0.053
			Low plus High RH	467	7.18	0.14 --	0.059
16-14	Fasting Glucose (mg/dl)[b]	0.089	Comparison	1,212	101.6		
			Background RH	381	100.3	–1.3 --	0.298
			Low RH	238	100.8	–0.8 --	0.618
			High RH	242	103.9	2.3 --	0.121
			Low plus High RH	480	102.4	0.8 --	0.485
16-16	2-Hour Postprandial Glucose (mg/dl)[b]	0.066	Comparison	996	104.7		
			Background RH	342	105.3	0.6 --	0.718
			Low RH	186	107.1	2.4 --	0.296
			High RH	183	104.5	–0.2 --	0.942
			Low plus High RH	369	105.8	1.1 --	0.521
16-20	Serum Insulin (μIU/ml)[b]	0.122	Comparison	996	47.35		
			Background RH	342	45.29	–2.06 --	0.393
			Low RH	186	51.97	4.62 --	0.157
			High RH	183	52.74	5.36 --	0.105
			Low plus High RH	369	52.35	5.00 --	0.046
16-22	α-1-C Hemoglobin (percent)[b]	0.087	Comparison	1,212	6.48		
			Background RH	381	6.38	–0.10 --	0.116
			Low RH	238	6.44	–0.04 --	0.588
			High RH	242	6.70	0.22 --	0.005
			Low plus High RH	480	6.57	0.09 --	0.138
16-24	Total Testosterone (ng/dl)[d]	0.121	Comparison	1,189	423.0		
			Background RH	372	429.8	6.8 --	0.499
			Low RH	234	404.6	–18.4 --	0.118
			High RH	238	429.4	6.4 --	0.592
			Low plus High RH	472	417.0	–6.0 --	0.508

Table G-3. Summary of Unadjusted Results for Continuous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Adj. Mean[a]	Difference of Means vs. Comparisons (95% C.I.)	p-Value
16-26	Free Testosterone (pg/ml)[d]	0.085	Comparison	1,189	13.95		
			Background RH	372	13.85	–0.10 --	0.703
			Low RH	234	13.23	–0.72 --	0.022
			High RH	238	14.85	0.90 --	0.006
			Low plus High RH	472	14.03	0.08 --	0.745
16-28	Estradiol (pg/ml)[d]	0.003	Comparison	1,213	40.68		
			Background RH	381	39.71	–0.97 --	0.323
			Low RH	239	39.58	–1.10 --	0.350
			High RH	243	41.43	0.75 --	0.523
			Low plus High RH	482	40.51	–0.17 --	0.852
16-30	LH (mIU/ml)[b]	0.003	Comparison	1,213	3.85		
			Background RH	381	4.01	0.16 --	0.264
			Low RH	239	3.83	–0.02 --	0.900
			High RH	243	3.74	–0.11 --	0.504
			Low plus High RH	482	3.78	–0.07 --	0.601
16-32	FSH (mIU/ml)[b]	0.002	Comparison	1,213	5.97		
			Background RH	381	6.21	0.24 --	0.283
			Low RH	239	6.28	0.31 --	0.258
			High RH	243	5.66	–0.31 --	0.229
			Low plus High RH	482	5.96	–0.01 --	0.955
17-4	CD3+ Cells (T Cells) (cells/mm^3)[b]	0.005	Comparison	440	1,252.1		
			Background RH	142	1,220.8	–31.3 --	0.490
			Low RH	84	1,225.9	–26.2 --	0.636
			High RH	91	1,242.7	–9.4 --	0.862
			Low plus High RH	175	1,234.6	–17.5 --	0.676
17-5	CD4+ Cells (Helper T Cells) (cells/mm^3)[b]	0.006	Comparison	440	854.9		
			Background RH	142	830.4	–24.5 --	0.421
			Low RH	84	835.6	–19.3 --	0.605
			High RH	91	862.2	7.3 --	0.842
			Low plus High RH	175	849.3	–5.6 --	0.844

Table G-3. Summary of Unadjusted Results for Continuous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Adj. Mean[a]	Difference of Means vs. Comparisons (95% C.I.)	p-Value
17-6	CD8+ Cells (Suppressor T Cells) (cells/mm^3)[b]	0.002	Comparison	440	584.1		
			Background RH	142	565.3	–18.8 --	0.479
			Low RH	84	571.8	–12.3 --	0.706
			High RH	91	552.4	–31.7 --	0.307
			Low plus High RH	175	561.6	–22.5 --	0.355
17-7	CD16+56+ Cells (Natural Killer Cells) (cells/mm^3)[b]	0.018	Comparison	440	275.4		
			Background RH	142	258.9	–16.5 --	0.192
			Low RH	84	281.1	5.7 --	0.726
			High RH	91	243.3	–32.1 --	0.028
			Low plus High RH	175	260.7	–14.7 --	0.209
17-8	CD20+ Cells (B Cells) (cells/mm^3)[b]	0.005	Comparison	440	185.0		
			Background RH	142	183.9	–1.1 --	0.918
			Low RH	83	166.7	–18.3 --	0.141
			High RH	91	195.5	10.5 --	0.419
			Low plus High RH	174	181.1	–3.9 --	0.694
17-9	CD3+CD4+ Cells (Helper T Cells) (cells/mm^3)[b]	0.005	Comparison	440	778.6		
			Background RH	142	753.7	–24.9 --	0.395
			Low RH	84	761.5	–17.1 --	0.632
			High RH	91	790.8	12.2 --	0.731
			Low plus High RH	175	776.6	–2.0 --	0.940
17-10	Absolute Lymphocytes (cells/mm^3)[b]	0.005	Comparison	1,164	1,775.7		
			Background RH	371	1,786.3	10.6 --	0.777
			Low RH	222	1,752.0	–23.7 --	0.598
			High RH	231	1,794.5	18.8 --	0.676
			Low plus High RH	453	1,773.5	–2.2 --	0.959
17-11	IgA (mg/dl)[b]	0.004	Comparison	1,164	233.6		
			Background RH	371	226.8	–6.8 --	0.297
			Low RH	222	232.3	–1.3 --	0.868
			High RH	231	240.9	7.3 --	0.373
			Low plus High RH	453	236.6	3.0 --	0.629

Table G-3. *Summary of Unadjusted Results for Continuous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)*

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Adj. Mean[a]	Difference of Means vs. Comparisons (95% C.I.)	p-Value
17-12	IgG (mg/dl)[b]	0.002	Comparison	1,164	1,048.1		
			Background RH	371	1,031.9	–16.2 --	0.254
			Low RH	222	1,041.7	–6.4 --	0.713
			High RH	231	1,039.6	–8.5 --	0.621
			Low plus High RH	453	1,040.7	–7.4 --	0.572
17-13	IgM (mg/dl)[b]	0.004	Comparison	1,164	98.2		
			Background RH	371	96.1	–2.1 --	0.487
			Low RH	222	95.8	–2.4 --	0.525
			High RH	231	96.4	–1.8 --	0.619
			Low plus High RH	453	96.1	–2.1 --	0.459
18-8	FVC (percent of predicted)	0.039	Comparison	1,211	99.14		
			Background RH	381	99.33	0.19 (–1.50,1.88)	0.825
			Low RH	238	98.34	–0.80 (–2.83,1.23)	0.439
			High RH	243	99.79	0.66 (–1.36,2.67)	0.523
			Low plus High RH	481	99.07	–0.06 (–1.61,1.48)	0.935
18-9	FEV_1 (percent of predicted)	0.003	Comparison	1,211	94.38		
			Background RH	381	93.94	–0.44 (–2.46,1.57)	0.668
			Low RH	238	92.89	–1.48 (–3.90,0.93)	0.229
			High RH	243	95.50	1.12 (–1.28,3.53)	0.360
			Low plus High RH	481	94.21	–0.17 (–2.01,1.67)	0.859
18-10	Observed FEV_1 to Observed FVC[c]	0.034	Comparison	1,211	0.763		
			Background RH	381	0.757	–0.006 --	0.192
			Low RH	238	0.757	–0.006 --	0.341
			High RH	243	0.770	0.007 --	0.164
			Low plus High RH	481	0.764	0.001 --	0.764

[a] Adjusted for percent body fat at the time of the blood measurement for dioxin.
[b] Means transformed from natural logarithm scale; difference of means after transformation to original scale; confidence interval not given because analysis was performed on natural logarithm scale; p-value based on difference of means on natural logarithm scale.

Table G-3. Summary of Unadjusted Results for Continuous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

[c] Means transformed from natural logarithm (clinical parameter + 0.1) scale; difference of means after transformation to original scale; confidence interval not given because analysis was performed on natural logarithm (clinical parameter + 0.1) scale; p-value based on difference of means on natural logarithm (clinical parameter + 0.1) scale.

[d] Means transformed from square root scale; difference of means after transformation to original scale; confidence interval not given because analysis was performed on square root scale; p-value based on difference of means on square root scale.

[e] Means transformed from natural logarithm (1 – clinical parameter) scale; difference of means after transformation to original scale; confidence interval not given because analysis was performed on natural logarithm (1 – clinical parameter) scale; p-value based on difference of means on natural logarithm (1 – clinical parameter) scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background: (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table G-4. Summary of Unadjusted Results for Continuous Variables – Model 4 (Ranch Hands: Log_2 (1987 Dioxin + 1))

Table Ref.	Clinical Parameter (Units)	R^2	Slope (Standard Error)	p-Value
9-6	Body Fat (percent) [a]	0.072	0.046 (0.006)	<0.001
9-8	Erythrocyte Sedimentation Rate (mm/hr) [b]	0.009	0.063 (0.022)	0.004
10-35	PSA (ng/ml) [a]	0.005	–0.037 (0.018)	0.043
13-11	AST (U/l) [a]	0.005	0.017 (0.008)	0.033
13-13	ALT (U/l) [a]	0.023	0.029 (0.007)	<0.001
13-15	GGT (U/l) [a]	0.012	0.040 (0.013)	0.002
13-17	Alkaline Phosphatase (U/l) [a]	<0.001	–0.004 (0.006)	0.555
13-19	Total Bilirubin (mg/dl) [a]	0.001	–0.007 (0.011)	0.499
13-22	Lactic Dehydrogenase (U/l) [a]	0.002	0.005 (0.004)	0.211
13-24	Cholesterol (mg/dl) [c]	0.008	0.077 (0.030)	0.009
13-26	HDL Cholesterol (mg/dl) [a]	0.016	–0.023 (0.006)	<0.001
13-28	Cholesterol-HDL Ratio [a]	0.030	0.033 (0.007)	<0.001
13-30	Triglycerides (mg/dl) [a]	0.028	0.072 (0.015)	<0.001
13-32	Creatine Phosphokinase (U/l) [a]	0.004	0.024 (0.014)	0.084
13-34	Serum Amylase (U/l) [a]	0.005	–0.019 (0.009)	0.035
13-41	Prealbumin (mg/dl)	<0.001	–0.047 (0.124)	0.704
13-43	Albumin (mg/dl)	<0.001	–2.471 (7.678)	0.748
13-45	α-1-Acid Glycoprotein (mg/dl) [a]	0.001	0.005 (0.005)	0.336
13-47	α-1-Antitrypsin (mg/dl) [c]	0.003	0.040 (0.025)	0.109
13-49	α-2-Macroglobulin (mg/dl) [a]	<0.001	–0.004 (0.006)	0.522
13-51	Apolipoprotein B (mg/dl) [c]	0.011	0.083 (0.027)	0.002
13-53	C3 Complement (mg/dl) [a]	0.040	0.021 (0.004)	<0.001
13-55	C4 Complement (mg/dl) [a]	0.004	0.009 (0.005)	0.070
13-57	Haptoglobin (mg/dl) [c]	0.002	0.074 (0.065)	0.254
13-59	Transferrin (mg/dl) [a]	0.004	0.005 (0.003)	0.082
14-7	Systolic Blood Pressure (mm Hg) [a]	<0.001	0.001 (0.003)	0.693
14-9	Diastolic Blood Pressure (mm Hg) [c]	0.007	0.031 (0.013)	0.014
15-3	RBC Count (million/mm^3)	0.003	0.013 (0.009)	0.136
15-5	WBC Count (thousand/mm^3) [a]	0.007	0.015 (0.006)	0.013
15-7	Hemoglobin (gm/dl)	0.003	0.035 (0.023)	0.133
15-9	Hematocrit (percent)	0.001	0.077 (0.071)	0.278
15-11	Platelet Count (thousand/mm^3) [c]	0.009	0.109 (0.039)	0.005
15-13	Prothrombin Time (seconds) [a]	0.002	–0.002 (0.002)	0.220
15-16	Absolute Neutrophils (segs) (thousand/mm^3) [a]	0.007	0.020 (0.008)	0.017
15-17	Absolute Neutrophils (bands) (Nonzero Measurements) (thousand/mm^3) [a]	0.001	0.015 (0.021)	0.482
15-19	Absolute Lymphocytes (thousand/mm^3) [a]	0.002	0.009 (0.008)	0.239
15-20	Absolute Monocytes (thousand/mm^3) [c]	0.004	0.007 (0.004)	0.059
15-21	Absolute Eosinophils (Nonzero Measurements) (thousand/mm^3) [a]	0.001	–0.017 (0.017)	0.330
15-23	Absolute Basophils (Nonzero Measurements) (thousand/mm^3) [a]	<0.001	0.006 (0.014)	0.674
16-6	Time to Diabetes Onset (years) [d]	--	–0.098 (0.021)	<0.001
16-9	TSH (μIU/ml) [a]	<0.001	–0.000 (0.015)	0.977
16-11	Thyroxine (μg/dl) [c]	0.008	0.015 (0.006)	0.009
16-14	Fasting Glucose (mg/dl) [a]	0.019	0.020 (0.005)	<0.001

Table G-4. Summary of Unadjusted Results for Continuous Variables – Model 4 (Ranch Hands: Log₂ (1987 Dioxin + 1)) (Continued)

Table Ref.	Clinical Parameter (Units)	R^2	Slope (Standard Error)	p-Value
16-16	2-Hour Postprandial Glucose (mg/dl)[a]	0.003	0.011 (0.007)	0.115
16-20	Serum Insulin (μIU/ml)[a]	0.025	0.100 (0.023)	<0.001
16-22	α-1-C Hemoglobin (percent)[a]	0.033	0.021 (0.004)	<0.001
16-24	Total Testosterone (ng/dl)[c]	0.010	–0.296 (0.101)	0.003
16-26	Free Testosterone (pg/ml)[c]	0.001	–0.010 (0.015)	0.489
16-28	Estradiol (pg/ml)[c]	0.002	0.039 (0.031)	0.212
16-30	LH (mIU/ml)[a]	0.005	–0.030 (0.015)	0.042
16-32	FSH (mIU/ml)[a]	0.003	–0.024 (0.015)	0.105
17-4	CD3+ Cells (T Cells) (cells/mm^3)[a]	0.003	0.015 (0.015)	0.316
17-5	CD4+ Cells (Helper T Cells) (cells/mm^3)[a]	0.004	0.017 (0.015)	0.255
17-6	CD8+ Cells (Suppressor T Cells) (cells/mm^3)[a]	0.001	0.009 (0.019)	0.640
17-7	CD16+56+ Cells (Natural Killer Cells) (cells/mm^3)[a]	<0.001	0.006 (0.021)	0.772
17-8	CD20+ Cells (B Cells) (cells/mm^3)[a]	0.004	0.026 (0.023)	0.260
17-9	CD3+CD4+ Cells (Helper T Cells) (cells/mm^3)[a]	0.005	0.019 (0.016)	0.228
17-10	Absolute Lymphocytes (cells/mm^3)[a]	0.002	0.010 (0.008)	0.222
17-11	IgA (mg/dl)[a]	0.005	0.022 (0.011)	0.051
17-12	IgG (mg/dl)[a]	<0.001	0.002 (0.005)	0.652
17-13	IgM (mg/dl)[a]	<0.001	–0.001 (0.012)	0.937
18-8	FVC (percent of predicted)	0.001	–0.312 (0.338)	0.356
18-9	FEV_1 (percent of predicted)	0.002	0.496 (0.402)	0.217
18-10	Observed FEV_1 to Observed FVC[e]	0.018	–0.031 (0.008)	<0.001

[a] Slope and standard error based on natural logarithm of clinical parameter versus $\log_2$ (initial dioxin).
[b] Slope and standard error based on natural logarithm of (clinical parameter + 0.1) versus $\log_2$ (initial dioxin).
[c] Slope and standard error based on square root of clinical parameter versus $\log_2$ (initial dioxin).
[d] Slope and standard error based on time to diabetes onset versus $\log_2$ (initial dioxin) under a censored Weibull distribution.
[e] Slope and standard error based on natural logarithm of (1 – clinical parameter) versus $\log_2$ (initial dioxin).
--: R-squared not presented because analysis was based on a censored Weibull distribution.

Table G-5. Summary of Unadjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons)

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal RH	Number (%) Abnormal C	Est. Relative Risk (95% C.I.)	p-Value
9-3	Self-perception of Health	All	124 (14.3)	130 (10.4)	1.44 (1.10,1.87)	0.007
		Officer	30 (8.8)	34 (6.9)	1.31 (0.78,2.18)	0.308
		Enlisted Flyer	26 (17.2)	23 (12.3)	1.48 (0.81,2.72)	0.203
		Enlisted Groundcrew	68 (18.0)	73 (12.8)	1.50 (1.05,2.15)	0.028
9-4	Appearance of Illness or Distress	All	15 (1.7)	14 (1.1)	1.55 (0.74,3.23)	0.242
		Officer	3 (0.9)	4 (0.8)	1.09 (0.24,4.89)	0.913
		Enlisted Flyer	3 (2.0)	2 (1.1)	1.87 (0.31,11.37)	0.494
		Enlisted Groundcrew	9 (2.4)	8 (1.4)	1.71 (0.66,4.48)	0.272
9-5	Relative Age Appearance	All	90 (10.3)	104 (8.3)	1.27 (0.95,1.71)	0.112
		Officer	22 (6.5)	25 (5.1)	1.29 (0.72,2.33)	0.392
		Enlisted Flyer	22 (14.6)	21 (11.2)	1.35 (0.71,2.56)	0.361
		Enlisted Groundcrew	46 (12.2)	58 (10.2)	1.22 (0.81,1.84)	0.337
9-7	Body Fat	All	244 (28.1)	376 (30.1)	0.91 (0.75,1.10)	0.316
		Officer	88 (25.8)	123 (24.9)	1.05 (0.76,1.44)	0.767
		Enlisted Flyer	37 (24.5)	58 (31.0)	0.72 (0.45,1.17)	0.186
		Enlisted Groundcrew	119 (31.5)	195 (34.2)	0.88 (0.67,1.17)	0.382
9-9	Erythrocyte Sedimentation Rate	All	72 (8.3)	88 (7.0)	1.19 (0.86,1.65)	0.289
		Officer	20 (5.9)	34 (6.9)	0.84 (0.48,1.49)	0.557
		Enlisted Flyer	17 (11.3)	14 (7.5)	1.57 (0.75,3.29)	0.235
		Enlisted Groundcrew	35 (9.3)	40 (7.0)	1.35 (0.84,2.17)	0.212
10-3	Skin Neoplasms	All	325 (40.4)	402 (34.4)	1.29 (1.07,1.55)	0.007
		Officer	150 (45.6)	183 (38.1)	1.36 (1.02,1.81)	0.034
		Enlisted Flyer	56 (40.0)	50 (28.9)	1.64 (1.02,2.63)	0.040
		Enlisted Groundcrew	119 (35.4)	169 (32.8)	1.12 (0.84,1.50)	0.433
10-4	Malignant Skin Neoplasms	All	144 (17.9)	187 (16.0)	1.14 (0.90,1.45)	0.274
		Officer	77 (23.4)	95 (19.8)	1.24 (0.88,1.74)	0.218
		Enlisted Flyer	29 (20.7)	22 (12.7)	1.79 (0.98,3.29)	0.059
		Enlisted Groundcrew	38 (11.3)	70 (13.6)	0.81 (0.53,1.24)	0.329
10-5	Benign Skin Neoplasms	All	225 (26.2)	264 (21.3)	1.31 (1.07,1.61)	0.010
		Officer	96 (28.6)	107 (22.0)	1.42 (1.03,1.96)	0.031
		Enlisted Flyer	34 (22.7)	32 (17.3)	1.40 (0.82,2.40)	0.220
		Enlisted Groundcrew	95 (25.4)	125 (22.0)	1.21 (0.89,1.64)	0.229
10-6	Skin Neoplasms of Uncertain Behavior or Unspecified Nature	All	7 (0.9)	8 (0.7)	1.27 (0.46,3.52)	0.645
		Officer	0 (0.0)	3 (0.6)	--	0.397[a]
		Enlisted Flyer	0 (0.0)	1 (0.6)	--	0.999[a]
		Enlisted Groundcrew	7 (2.1)	4 (0.8)	2.72 (0.79,9.36)	0.113
10-7	Basal Cell Carcinoma	All	121 (15.0)	155 (13.3)	1.16 (0.89,1.49)	0.269
		Officer	67 (20.4)	80 (16.7)	1.28 (0.89,1.83)	0.181
		Enlisted Flyer	26 (18.6)	19 (11.0)	1.85 (0.98,3.50)	0.060
		Enlisted Groundcrew	28 (8.3)	56 (10.9)	0.75 (0.46,1.20)	0.226

Table G-5. Summary of Unadjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal RH	Number (%) Abnormal C	Est. Relative Risk (95% C.I.)	p-Value
10-8	Basal Cell Carcinoma (Ear, Face, Head, and Neck)	All	93 (11.6)	120 (10.3)	1.14 (0.86,1.52)	0.370
		Officer	49 (14.9)	60 (12.5)	1.23 (0.82,1.84)	0.328
		Enlisted Flyer	22 (15.7)	17 (9.8)	1.71 (0.87,3.37)	0.120
		Enlisted Groundcrew	22 (6.6)	43 (8.4)	0.77 (0.45,1.31)	0.334
10-9	Basal Cell Carcinoma (Trunk)	All	40 (5.0)	47 (4.0)	1.25 (0.81,1.92)	0.318
		Officer	29 (8.8)	29 (6.0)	1.50 (0.88,2.57)	0.135
		Enlisted Flyer	6 (4.3)	3 (1.7)	2.54 (0.62,10.33)	0.194
		Enlisted Groundcrew	5 (1.5)	15 (2.9)	0.50 (0.18,1.40)	0.188
10-10	Basal Cell Carcinoma (Upper Extremities)	All	21 (2.6)	38 (3.3)	0.80 (0.46,1.37)	0.405
		Officer	17 (5.2)	24 (5.0)	1.04 (0.55,1.96)	0.915
		Enlisted Flyer	1 (0.7)	2 (1.2)	0.62 (0.06,6.85)	0.693
		Enlisted Groundcrew	3 (0.9)	12 (2.3)	0.38 (0.11,1.35)	0.134
10-11	Basal Cell Carcinoma (Lower Extremities)	All	5 (0.6)	5 (0.4)	1.45 (0.42,5.04)	0.556
		Officer	4 (1.2)	3 (0.6)	1.96 (0.44,8.80)	0.381
		Enlisted Flyer	0 (0.0)	0 (0.0)	--	--
		Enlisted Groundcrew	1 (0.3)	2 (0.4)	0.77 (0.07,8.48)	0.828
10-12	Squamous Cell Carcinoma	All	20 (2.5)	22 (1.9)	1.33 (0.72,2.45)	0.367
		Officer	11 (3.3)	16 (3.3)	1.00 (0.46,2.19)	0.994
		Enlisted Flyer	3 (2.1)	2 (1.2)	1.87 (0.31,11.36)	0.495
		Enlisted Groundcrew	6 (1.8)	4 (0.8)	2.32 (0.65,8.29)	0.194
10-13	Nonmelanoma	All	134 (16.7)	176 (15.1)	1.13 (0.88,1.44)	0.345
		Officer	73 (22.2)	89 (18.5)	1.25 (0.89,1.77)	0.203
		Enlisted Flyer	29 (20.7)	21 (12.1)	1.89 (1.02,3.49)	0.042
		Enlisted Groundcrew	32 (9.5)	66 (12.8)	0.72 (0.46,1.12)	0.143
10-14	Melanoma	All	16 (2.0)	13 (1.1)	1.80 (0.86.3.77)	0.117
		Officer	9 (2.7)	7 (1.5)	1.90 (0.70,5.16)	0.207
		Enlisted Flyer	0 (0.0)	1 (0.6)	--	0.999[a]
		Enlisted Groundcrew	7 (2.1)	5 (1.0)	2.17 (0.68,6.90)	0.189
10-15	Systemic Neoplasms (All Sites Combined)	All	267 (31.2)	370 (29.8)	1.07 (0.89,1.29)	0.482
		Officer	110 (33.1)	168 (34.4)	0.95 (0.70,1.27)	0.716
		Enlisted Flyer	49 (33.3)	55 (29.4)	1.20 (0.75,1.91)	0.443
		Enlisted Groundcrew	108 (28.7)	147 (26.0)	1.15 (0.86,1.54)	0.352
10-16	Malignant Systemic Neoplasms	All	67 (7.8)	75 (6.0)	1.32 (0.94,1.86)	0.112
		Officer	32 (9.6)	39 (7.9)	1.23 (0.76,2.01)	0.403
		Enlisted Flyer	18 (12.1)	11 (5.9)	2.20 (1.00,4.81)	0.049
		Enlisted Groundcrew	17 (4.5)	25 (4.4)	1.03 (0.55,1.93)	0.937
10-17	Benign Systemic Neoplasms	All	217 (25.4)	299 (24.1)	1.07 (0.88,1.31)	0.495
		Officer	82 (24.7)	130 (26.6)	0.91 (0.66,1.25)	0.545
		Enlisted Flyer	40 (27.2)	47 (25.1)	1.11 (0.68,1.82)	0.668
		Enlisted Groundcrew	95 (25.3)	122 (21.6)	1.23 (0.91,1.67)	0.186

Table G-5. Summary of Unadjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal RH	Number (%) Abnormal C	Est. Relative Risk (95% C.I.)	p-Value
10-18	Systemic Neoplasms of Uncertain Behavior or Unspecified Nature	All	16 (1.9)	25 (2.0)	0.93 (0.49,1.75)	0.814
		Officer	11 (3.3)	13 (2.6)	1.26 (0.56,2.84)	0.583
		Enlisted Flyer	1 (0.7)	2 (1.1)	0.63 (0.06,6.96)	0.702
		Enlisted Groundcrew	4 (1.1)	10 (1.8)	0.60 (0.19,1.92)	0.388
10-19	Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck)	All	9 (1.1)	12 (1.0)	1.09 (0.46,2.60)	0.848
		Officer	6 (1.8)	4 (0.8)	2.23 (0.63,7.98)	0.216
		Enlisted Flyer	1 (0.7)	3 (1.6)	0.41 (0.04,4.03)	0.448
		Enlisted Groundcrew	2 (0.5)	5 (0.9)	0.60 (0.12,3.11)	0.543
10-20	Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx)	All	4 (0.5)	7 (0.6)	0.83 (0.24,2.84)	0.762
		Officer	2 (0.6)	2 (0.4)	1.48 (0.21,10.54)	0.697
		Enlisted Flyer	1 (0.7)	2 (1.1)	0.63 (0.06,6.96)	0.702
		Enlisted Groundcrew	1 (0.3)	3 (0.5)	0.50 (0.05,4.83)	0.550
10-21	Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum)	All	2 (0.2)	0 (0.0)	--	0.325[a]
		Officer	1 (0.3)	0 (0.0)	--	0.845[a]
		Enlisted Flyer	0 (0.0)	0 (0.0)	--	--
		Enlisted Groundcrew	1 (0.3)	0 (0.0)	--	0.836[a]
10-22	Malignant Systemic Neoplasms (Thyroid Gland)	All	2 (0.2)	2 (0.2)	1.45 (0.20,10.33)	0.710
		Officer	2 (0.6)	1 (0.2)	2.96 (0.27,32.79)	0.376
		Enlisted Flyer	0 (0.0)	0 (0.0)	--	--
		Enlisted Groundcrew	0 (0.0)	1 (0.2)	--	0.999[a]
10-23	Malignant Systemic Neoplasms (Bronchus and Lung)	All	10 (1.2)	3 (0.2)	4.88 (1.34,17.79)	0.008
		Officer	5 (1.5)	2 (0.4)	3.73 (0.72,19.33)	0.117
		Enlisted Flyer	3 (2.0)	1 (0.5)	3.82 (0.39,37.13)	0.248
		Enlisted Groundcrew	2 (0.5)	0 (0.0)	--	0.310[a]
10-24	Malignant Systemic Neoplasms (Liver)	All	2 (0.2)	2 (0.2)	1.45 (0.20,10.33)	0.710
		Officer	0 (0.0)	1 (0.2)	--	0.999[a]
		Enlisted Flyer	1 (0.7)	0 (0.0)	--	0.909[a]
		Enlisted Groundcrew	1 (0.3)	1 (0.2)	1.51 (0.09,24.18)	0.772
10-25	Malignant Systemic Neoplasms (Colon and Rectum)	All	7 (0.8)	8 (0.6)	1.27 (0.46,3.52)	0.645
		Officer	3 (0.9)	2 (0.4)	2.22 (0.37,13.38)	0.383
		Enlisted Flyer	2 (1.3)	2 (1.1)	1.26 (0.18,9.04)	0.819
		Enlisted Groundcrew	2 (0.5)	4 (0.7)	0.75 (0.14,4.13)	0.743
10-26	Malignant Systemic Neoplasms (Kidney and Bladder)	All	11 (1.3)	6 (0.5)	2.68 (0.99,7.28)	0.046
		Officer	5 (1.5)	5 (1.0)	1.48 (0.43,5.16)	0.537
		Enlisted Flyer	3 (2.0)	0 (0.0)	--	0.172[a]
		Enlisted Groundcrew	3 (0.8)	1 (0.2)	4.55 (0.47,43.89)	0.190
10-27	Malignant Systemic Neoplasms (Prostate)	All	26 (3.0)	39 (3.1)	0.97 (0.58,1.60)	0.893
		Officer	13 (3.9)	25 (5.1)	0.76 (0.38,1.50)	0.427
		Enlisted Flyer	7 (4.7)	4 (2.1)	2.26 (0.65,7.86)	0.201
		Enlisted Groundcrew	6 (1.6)	10 (1.8)	0.90 (0.33,2.50)	0.844

Table G-5. Summary of Unadjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal RH	Number (%) Abnormal C	Est. Relative Risk (95% C.I.)	p-Value
10-28	Malignant Systemic Neoplasms (Testicles)	All	3 (0.4)	0 (0.0)	--	0.134[a]
		Officer	1 (0.3)	0 (0.0)	--	0.845[a]
		Enlisted Flyer	1 (0.7)	0 (0.0)	--	0.909[a]
		Enlisted Groundcrew	1 (0.3)	0 (0.0)	--	0.836[a]
10-29	Malignant Systemic Neoplasms (Connective and Other Soft Tissues)	All	1 (0.1)	2 (0.2)	0.73 (0.07,8.01)	0.790
		Officer	0 (0.0)	0 (0.0)	--	--
		Enlisted Flyer	1 (0.7)	0 (0.0)	--	0.909[a]
		Enlisted Groundcrew	0 (0.0)	2 (0.4)	--	0.667[a]
10-30	Hodgkin's Disease	All	1 (0.1)	3 (0.2)	0.48 (0.05,4.65)	0.507
		Officer	1 (0.3)	2 (0.4)	0.74 (0.07,8.16)	0.803
		Enlisted Flyer	0 (0.0)	0 (0.0)	--	--
		Enlisted Groundcrew	0 (0.0)	1 (0.2)	--	0.999[a]
10-31	Non-Hodgkin's Lymphoma	All	1 (0.1)	3 (0.2)	0.48 (0.05,4.65)	0.507
		Officer	0 (0.0)	2 (0.4)	--	0.657[a]
		Enlisted Flyer	0 (0.0)	0 (0.0)	--	--
		Enlisted Groundcrew	1 (0.3)	1 (0.2)	1.51 (0.09,24.18)	0.772
10-32	Other Malignant Systemic Neoplasms of Lymphoid and Histiocytic Tissue	All	2 (0.2)	4 (0.3)	0.72 (0.13,3.97)	0.706
		Officer	1 (0.3)	2 (0.4)	0.74 (0.07,8.16)	0.803
		Enlisted Flyer	0 (0.0)	1 (0.5)	--	0.999[a]
		Enlisted Groundcrew	1 (0.3)	1 (0.2)	1.51 (0.09,24.18)	0.772
10-33	Malignant Skin and Systemic Neoplasms	All	186 (21.9)	234 (18.9)	1.20 (0.97,1.49)	0.099
		Officer	95 (28.8)	116 (23.8)	1.29 (0.94,1.77)	0.112
		Enlisted Flyer	39 (26.4)	31 (16.8)	1.78 (1.04,3.02)	0.034
		Enlisted Groundcrew	52 (13.9)	87 (15.4)	0.89 (0.62,1.29)	0.546
10-34	All Skin and Systemic Neoplasms	All	473 (55.8)	620 (50.4)	1.25 (1.05,1.49)	0.014
		Officer	202 (61.4)	266 (55.2)	1.29 (0.97,1.72)	0.079
		Enlisted Flyer	84 (57.5)	92 (49.7)	1.37 (0.88,2.12)	0.158
		Enlisted Groundcrew	187 (50.3)	262 (46.5)	1.17 (0.90,1.51)	0.253
10-36	PSA	All	54 (6.5)	73 (6.1)	1.07 (0.74,1.53)	0.730
		Officer	31 (9.7)	29 (6.3)	1.59 (0.94,2.69)	0.086
		Enlisted Flyer	10 (7.1)	15 (8.3)	0.84 (0.37,1.93)	0.681
		Enlisted Groundcrew	13 (3.5)	29 (5.3)	0.66 (0.34,1.29)	0.223
11-3	Inflammatory Diseases	All	7 (0.8)	1 (0.1)	10.11 (1.24,82.35)	0.006
		Officer	2 (0.6)	0 (0.0)	--	0.327[a]
		Enlisted Flyer	2 (1.3)	0 (0.0)	--	0.391[a]
		Enlisted Groundcrew	3 (0.8)	1 (0.2)	4.56 (0.47,44.05)	0.189
11-4	Hereditary and Degenerative Diseases	All	80 (9.2)	108 (8.7)	1.08 (0.79,1.46)	0.639
		Officer	30 (8.8)	37 (7.5)	1.19 (0.72,1.97)	0.492
		Enlisted Flyer	19 (12.6)	19 (10.2)	1.27 (0.65,2.50)	0.484
		Enlisted Groundcrew	31 (8.3)	52 (9.1)	0.90 (0.56,1.43)	0.643

Table G-5. Summary of Unadjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal RH	Number (%) Abnormal C	Est. Relative Risk (95% C.I.)	p-Value
11-5	Peripheral Disorders	All	188 (21.8)	241 (19.3)	1.16 (0.94,1.44)	0.169
		Officer	78 (23.0)	91 (18.5)	1.32 (0.94,1.85)	0.113
		Enlisted Flyer	36 (24.0)	44 (23.7)	1.02 (0.62,1.69)	0.941
		Enlisted Groundcrew	74 (19.8)	106 (18.6)	1.08 (0.77,1.50)	0.658
11-6	Other Neurological Disorders	All	173 (20.1)	211 (17.0)	1.23 (0.98,1.54)	0.070
		Officer	29 (8.6)	38 (7.7)	1.12 (0.68,1.86)	0.656
		Enlisted Flyer	46 (30.5)	45 (24.2)	1.37 (0.85,2.22)	0.198
		Enlisted Groundcrew	98 (26.3)	128 (22.6)	1.22 (0.90,1.65)	0.200
11-7	Smell	All	20 (2.3)	19 (1.5)	1.54 (0.81,2.89)	0.186
		Officer	5 (1.5)	10 (2.0)	0.73 (0.25,2.14)	0.562
		Enlisted Flyer	6 (4.0)	1 (0.5)	7.70 (0.92,64.65)	0.060
		Enlisted Groundcrew	9 (2.4)	8 (1.4)	1.73 (0.66,4.51)	0.266
11-8	Visual Fields	All	2 (0.2)	5 (0.4)	0.57 (0.11,2.97)	0.493
		Officer	0 (0.0)	1 (0.2)	--	0.999[a]
		Enlisted Flyer	1 (0.7)	2 (1.1)	0.61 (0.06,6.83)	0.691
		Enlisted Groundcrew	1 (0.3)	2 (0.4)	0.76 (0.07,8.36)	0.819
11-9	Light Reaction	All	1 (0.1)	12 (1.0)	0.12 (0.02,0.92)	0.007
		Officer	0 (0.0)	3 (0.6)	--	0.399[a]
		Enlisted Flyer	1 (0.7)	4 (2.1)	0.31 (0.03,2.76)	0.291
		Enlisted Groundcrew	0 (0.0)	5 (0.9)	--	0.173[a]
11-10	Ocular Movement	All	14 (1.6)	17 (1.4)	1.19 (0.58,2.43)	0.632
		Officer	2 (0.6)	5 (1.0)	0.58 (0.11,2.99)	0.513
		Enlisted Flyer	3 (2.0)	2 (1.1)	1.87 (0.31,11.37)	0.494
		Enlisted Groundcrew	9 (2.4)	10 (1.8)	1.37 (0.55,3.42)	0.493
11-11	Facial Sensation	All	2 (0.2)	2 (0.2)	1.44 (0.20,10.27)	0.714
		Officer	1 (0.3)	1 (0.2)	1.46 (0.09,23.35)	0.791
		Enlisted Flyer	0 (0.0)	1 (0.5)	--	0.999[a]
		Enlisted Groundcrew	1 (0.3)	0 (0.0)	--	0.834[a]
11-12	Jaw Clench	All	2 (0.2)	0 (0.0)	--	0.327[a]
		Officer	2 (0.6)	0 (0.0)	--	0.325[a]
		Enlisted Flyer	0 (0.0)	0 (0.0)	--	--
		Enlisted Groundcrew	0 (0.0)	0 (0.0)	--	--
11-13	Smile	All	7 (0.8)	4 (0.3)	2.54 (0.74,8.69)	0.129
		Officer	1 (0.3)	2 (0.4)	0.72 (0.07,8.02)	0.793
		Enlisted Flyer	1 (0.7)	0 (0.0)	--	0.915[a]
		Enlisted Groundcrew	5 (1.3)	2 (0.4)	3.83 (0.74,19.85)	0.110
11-14	Palpebral Fissure	All	7 (0.8)	12 (1.0)	0.84 (0.33,2.14)	0.713
		Officer	2 (0.6)	5 (1.0)	0.58 (0.11,2.99)	0.513
		Enlisted Flyer	1 (0.7)	1 (0.5)	1.24 (0.08,19.99)	0.879
		Enlisted Groundcrew	4 (1.1)	6 (1.1)	1.01 (0.28,3.61)	0.986

Table G-5. Summary of Unadjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal RH	Number (%) Abnormal C	Est. Relative Risk (95% C.I.)	p-Value
11-15	Balance	All	7 (0.8)	7 (0.6)	1.44 (0.50,4.13)	0.494
		Officer	5 (1.5)	2 (0.4)	3.66 (0.71,19.00)	0.122
		Enlisted Flyer	0 (0.0)	1 (0.5)	--	0.999[a]
		Enlisted Groundcrew	2 (0.5)	4 (0.7)	0.76 (0.14,4.16)	0.749
11-16	Speech	All	4 (0.5)	10 (0.8)	0.57 (0.18,1.84)	0.334
		Officer	1 (0.3)	2 (0.4)	0.72 (0.07,8.02)	0.793
		Enlisted Flyer	0 (0.0)	1 (0.5)	--	0.999[a]
		Enlisted Groundcrew	3 (0.8)	7 (1.2)	0.65 (0.17,2.52)	0.531
11-17	Tongue Position Relative to Midline	All	2 (0.2)	0 (0.0)	--	0.327[a]
		Officer	2 (0.6)	0 (0.0)	--	0.325[a]
		Enlisted Flyer	0 (0.0)	0 (0.0)	--	--
		Enlisted Groundcrew	0 (0.0)	0 (0.0)	--	--
11-18	Palate and Uvula Movement	All	1 (0.1)	0 (0.0)	--	0.854[a]
		Officer	1 (0.3)	0 (0.0)	--	0.852[a]
		Enlisted Flyer	0 (0.0)	0 (0.0)	--	--
		Enlisted Groundcrew	0 (0.0)	0 (0.0)	--	--
11-19	Cranial Nerve Index	All	56 (6.6)	72 (5.8)	1.15 (0.80,1.65)	0.452
		Officer	17 (5.2)	26 (5.3)	0.98 (0.52,1.83)	0.941
		Enlisted Flyer	13 (8.6)	10 (5.4)	1.66 (0.71,3.89)	0.246
		Enlisted Groundcrew	26 (7.0)	36 (6.4)	1.11 (0.66,1.88)	0.683
11-20	Neck Range of Motion	All	165 (19.1)	188 (15.1)	1.33 (1.06,1.67)	0.016
		Officer	70 (20.6)	81 (16.4)	1.32 (0.92,1.88)	0.126
		Enlisted Flyer	41 (27.2)	29 (15.5)	2.03 (1.19,3.46)	0.009
		Enlisted Groundcrew	54 (14.4)	78 (13.7)	1.06 (0.73,1.54)	0.764
11-21	Pinprick	All	57 (6.9)	67 (5.7)	1.24 (0.86,1.79)	0.244
		Officer	20 (6.2)	22 (4.7)	1.35 (0.72,2.51)	0.350
		Enlisted Flyer	19 (13.1)	14 (7.7)	1.81 (0.87,3.75)	0.110
		Enlisted Groundcrew	18 (5.1)	31 (5.8)	0.87 (0.48,1.57)	0.638
11-22	Light Touch	All	38 (4.6)	45 (3.8)	1.23 (0.79,1.91)	0.363
		Officer	15 (4.7)	13 (2.8)	1.71 (0.80,3.65)	0.163
		Enlisted Flyer	12 (8.3)	10 (5.5)	1.55 (0.65,3.70)	0.322
		Enlisted Groundcrew	11 (3.1)	22 (4.1)	0.74 (0.36,1.55)	0.432
11-23	Muscle Status	All	39 (4.5)	37 (3.0)	1.54 (0.98,2.44)	0.064
		Officer	13 (3.8)	18 (3.7)	1.05 (0.51,2.17)	0.897
		Enlisted Flyer	10 (6.6)	7 (3.7)	1.82 (0.68,4.91)	0.235
		Enlisted Groundcrew	16 (4.3)	12 (2.1)	2.06 (0.97,4.42)	0.062
11-24	Patellar Reflex	All	24 (2.8)	35 (2.8)	0.99 (0.58,1.67)	0.962
		Officer	12 (3.5)	16 (3.3)	1.09 (0.51,2.34)	0.823
		Enlisted Flyer	1 (0.7)	7 (3.8)	0.17 (0.02,1.40)	0.100
		Enlisted Groundcrew	11 (2.9)	12 (2.1)	1.40 (0.61,3.21)	0.425

Table G-5. Summary of Unadjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal RH	Number (%) Abnormal C	Est. Relative Risk (95% C.I.)	p-Value
11-25	Achilles Reflex	All	153 (17.7)	203 (16.3)	1.10 (0.88,1.39)	0.410
		Officer	67 (19.7)	82 (16.7)	1.22 (0.86,1.75)	0.267
		Enlisted Flyer	30 (19.9)	37 (19.9)	1.00 (0.58,1.71)	0.995
		Enlisted Groundcrew	56 (15.0)	84 (14.8)	1.01 (0.70,1.46)	0.947
11-26	Biceps Reflex	All	12 (1.4)	12 (1.0)	1.45 (0.65,3.24)	0.369
		Officer	5 (1.5)	6 (1.2)	1.21 (0.37,4.00)	0.753
		Enlisted Flyer	2 (1.3)	2 (1.1)	1.24 (0.17,8.92)	0.830
		Enlisted Groundcrew	5 (1.3)	4 (0.7)	1.91 (0.51,7.14)	0.339
11-27	Babinski Reflex	All	8 (0.9)	13 (1.0)	0.88 (0.36,2.14)	0.785
		Officer	3 (0.9)	2 (0.4)	2.18 (0.36,13.12)	0.394
		Enlisted Flyer	1 (0.7)	3 (1.6)	0.40 (0.04,3.93)	0.435
		Enlisted Groundcrew	4 (1.1)	8 (1.4)	0.76 (0.23,2.53)	0.650
11-29	Polyneuropathy Prevalence Index	All	130 (15.8)	179 (15.1)	1.06 (0.83,1.35)	0.668
		Officer	55 (17.1)	75 (16.0)	1.08 (0.74,1.58)	0.694
		Enlisted Flyer	29 (20.0)	39 (21.4)	0.92 (0.53,1.57)	0.752
		Enlisted Groundcrew	46 (13.0)	65 (12.2)	1.08 (0.72,1.61)	0.725
11-30	Multiple Polyneuropathy Index	All	41 (5.0)	38 (3.2)	1.58 (1.01,2.49)	0.046
		Officer	16 (5.0)	17 (3.6)	1.39 (0.69,2.79)	0.358
		Enlisted Flyer	13 (9.0)	9 (5.0)	1.89 (0.79,4.56)	0.155
		Enlisted Groundcrew	12 (3.4)	12 (2.3)	1.52 (0.68,3.43)	0.309
11-31	Confirmed Polyneuropathy Indicator	All	11 (1.4)	7 (0.6)	2.30 (0.89,5.95)	0.082
		Officer	2 (0.6)	6 (1.3)	0.49 (0.10,2.43)	0.381
		Enlisted Flyer	4 (2.8)	0 (0.0)	--	0.079[a]
		Enlisted Groundcrew	5 (1.4)	1 (0.2)	7.62 (0.89,65.47)	0.064
11-32	Tremor	All	60 (6.9)	91 (7.3)	0.95 (0.68,1.33)	0.753
		Officer	22 (6.5)	29 (5.9)	1.11 (0.62,1.96)	0.728
		Enlisted Flyer	15 (9.9)	15 (8.0)	1.26 (0.60,2.68)	0.540
		Enlisted Groundcrew	23 (6.1)	47 (8.3)	0.73 (0.43,1.22)	0.224
11-33	Coordination	All	19 (2.2)	31 (2.5)	0.88 (0.49,1.57)	0.663
		Officer	10 (2.9)	8 (1.6)	1.84 (0.72,4.70)	0.205
		Enlisted Flyer	1 (0.7)	4 (2.2)	0.30 (0.03,2.74)	0.288
		Enlisted Groundcrew	8 (2.1)	19 (3.4)	0.63 (0.27,1.45)	0.279
11-34	Romberg Sign	All	7 (0.8)	7 (0.6)	1.44 (0.50,4.13)	0.494
		Officer	5 (1.5)	2 (0.4)	3.66 (0.71,19.00)	0.122
		Enlisted Flyer	0 (0.0)	1 (0.5)	--	0.999[a]
		Enlisted Groundcrew	2 (0.5)	4 (0.7)	0.76 (0.14,4.16)	0.749
11-35	Gait	All	50 (5.8)	57 (4.6)	1.28 (0.87,1.89)	0.214
		Officer	19 (5.6)	26 (5.3)	1.06 (0.58,1.95)	0.844
		Enlisted Flyer	11 (7.3)	11 (5.9)	1.26 (0.53,2.98)	0.604
		Enlisted Groundcrew	20 (5.3)	20 (3.5)	1.55 (0.82,2.92)	0.178

Table G-5. Summary of Unadjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal RH	Number (%) Abnormal C	Est. Relative Risk (95% C.I.)	p-Value
11-36	CNS Index	All	107 (12.4)	148 (11.9)	1.05 (0.80,1.37)	0.731
		Officer	39 (11.5)	53 (10.8)	1.08 (0.69,1.67)	0.745
		Enlisted Flyer	24 (15.9)	28 (15.0)	1.07 (0.59,1.94)	0.816
		Enlisted Groundcrew	44 (11.7)	67 (11.8)	0.99 (0.66,1.49)	0.977
12-3	Psychoses	All	34 (3.9)	48 (3.8)	1.02 (0.65,1.60)	0.927
		Officer	9 (2.6)	12 (2.4)	1.09 (0.45,2.61)	0.853
		Enlisted Flyer	10 (6.6)	7 (3.7)	1.82 (0.68,4.91)	0.235
		Enlisted Groundcrew	15 (4.0)	29 (5.1)	0.78 (0.41,1.47)	0.435
12-4	Alcohol Dependence	All	62 (7.2)	83 (6.7)	1.08 (0.77,1.52)	0.655
		Officer	15 (4.4)	26 (5.3)	0.83 (0.43,1.58)	0.566
		Enlisted Flyer	14 (9.3)	16 (8.6)	1.09 (0.52,2.32)	0.818
		Enlisted Groundcrew	33 (8.8)	41 (7.2)	1.24 (0.77,2.00)	0.377
12-5	Drug Dependence	All	2 (0.2)	4 (0.3)	0.72 (0.13,3.94)	0.700
		Officer	0 (0.0)	1 (0.2)	--	0.999[a]
		Enlisted Flyer	0 (0.0)	0 (0.0)	--	--
		Enlisted Groundcrew	2 (0.5)	3 (0.5)	1.01 (0.17,6.08)	0.990
12-6	Anxiety	All	232 (26.9)	334 (26.8)	1.00 (0.83,1.22)	0.969
		Officer	56 (16.5)	88 (17.9)	0.91 (0.63,1.31)	0.605
		Enlisted Flyer	48 (32.0)	56 (30.0)	1.10 (0.69,1.75)	0.685
		Enlisted Groundcrew	128 (34.3)	190 (33.6)	1.03 (0.78,1.36)	0.813
12-7	Other Neuroses	All	467 (54.6)	660 (53.2)	1.06 (0.89,1.26)	0.529
		Officer	136 (40.2)	226 (46.0)	0.79 (0.60,1.05)	0.099
		Enlisted Flyer	93 (62.4)	112 (60.5)	1.08 (0.69,1.69)	0.726
		Enlisted Groundcrew	238 (64.7)	322 (57.1)	1.38 (1.05,1.08)	0.021
12-8	SCL-90-R Anxiety	All	82 (9.5)	140 (11.2)	0.83 (0.62,1.10)	0.197
		Officer	14 (4.1)	28 (5.7)	0.71 (0.37,1.37)	0.309
		Enlisted Flyer	15 (10.0)	30 (16.0)	0.58 (0.30.1.13)	0.108
		Enlisted Groundcrew	53 (14.1)	82 (14.4)	0.98 (0.67,1.42)	0.905
12-9	SCL-90-R Depression	All	115 (13.3)	201 (16.1)	0.80 (0.62,1.02)	0.073
		Officer	28 (8.2)	47 (9.5)	0.85 (0.52,1.39)	0.512
		Enlisted Flyer	19 (12.7)	40 (21.4)	0.53 (0.29,0.97)	0.038
		Enlisted Groundcrew	68 (18.1)	114 (20.0)	0.88 (0.63,1.23)	0.469
12-10	SCL-90-R Hostility	All	61 (7.0)	111 (8.9)	0.78 (0.56,1.08)	0.124
		Officer	11 (3.2)	23 (4.7)	0.68 (0.33,1.42)	0.304
		Enlisted Flyer	11 (7.3)	21 (11.2)	0.63 (0.29,1.34)	0.228
		Enlisted Groundcrew	39 (10.4)	67 (11.8)	0.87 (0.57,1.32)	0.513
12-11	SCL-90-R Interpersonal Sensitivity	All	117 (13.5)	205 (16.4)	0.80 (0.62,1.02)	0.066
		Officer	25 (7.3)	40 (8.1)	0.90 (0.53,1.51)	0.679
		Enlisted Flyer	22 (14.7)	42 (22.5)	0.59 (0.34,1.05)	0.072
		Enlisted Groundcrew	70 (18.7)	123 (21.6)	0.83 (0.60,1.15)	0.272

Table G-5. Summary of Unadjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal RH	Number (%) Abnormal C	Est. Relative Risk (95% C.I.)	p-Value
12-12	SCL-90-R Obsessive-Compulsive Behavior	All	121 (14.0)	205 (16.4)	0.83 (0.65,1.06)	0.125
		Officer	30 (8.8)	47 (9.5)	0.92 (0.57,1.48)	0.718
		Enlisted Flyer	28 (18.7)	41 (21.9)	0.82 (0.48,1.40)	0.462
		Enlisted Groundcrew	63 (16.8)	117 (20.6)	0.78 (0.56,1.09)	0.150
12-13	SCL-90-R Paranoid Ideation	All	57 (6.6)	89 (7.1)	0.92 (0.65,1.30)	0.627
		Officer	8 (2.4)	15 (3.0)	0.77 (0.32,1.83)	0.547
		Enlisted Flyer	8 (5.3)	17 (9.1)	0.56 (0.24,1.34)	0.196
		Enlisted Groundcrew	41 (10.9)	57 (10.0)	1.10 (0.72,1.69)	0.652
12-14	SCL-90-R Phobic Anxiety	All	85 (9.8)	131 (10.5)	0.93 (0.70,1.24)	0.615
		Officer	10 (2.9)	28 (5.7)	0.50 (0.24,1.05)	0.066
		Enlisted Flyer	15 (10.0)	27 (14.4)	0.66 (0.34,1.29)	0.223
		Enlisted Groundcrew	60 (16.0)	76 (13.4)	1.24 (0.86,1.78)	0.258
12-15	SCL-90-R Psychoticism	All	105 (12.1)	184 (14.7)	0.80 (0.62,1.03)	0.084
		Officer	21 (6.2)	45 (9.1)	0.65 (0.38,1.12)	0.121
		Enlisted Flyer	19 (12.7)	31 (16.6)	0.73 (0.39,1.35)	0.317
		Enlisted Groundcrew	65 (17.3)	108 (19.0)	0.90 (0.64,1.26)	0.522
12-16	SCL-90-R Somatization	All	143 (16.5)	201 (16.1)	1.03 (0.82,1.30)	0.797
		Officer	25 (7.3)	36 (7.3)	1.00 (0.59,1.71)	0.987
		Enlisted Flyer	33 (22.0)	52 (27.8)	0.73 (0.44,1.21)	0.223
		Enlisted Groundcrew	85 (22.7)	113 (19.9)	1.18 (0.86,1.62)	0.300
12-17	SCL-90-R Global Severity Index (GSI)	All	118 (13.6)	195 (15.6)	0.85 (0.67,1.09)	0.204
		Officer	23 (6.7)	37 (7.5)	0.89 (0.52,1.53)	0.676
		Enlisted Flyer	22 (14.7)	41 (21.9)	0.61 (0.35,1.08)	0.091
		Enlisted Groundcrew	73 (19.5)	117 (20.6)	0.93 (0.67,1.29)	0.681
12-18	SCL-90-R Positive Symptom Total (PST)	All	123 (14.2)	213 (17.1)	0.81 (0.63,1.02)	0.076
		Officer	25 (7.3)	46 (9.3)	0.77 (0.46,1.28)	0.310
		Enlisted Flyer	26 (17.3)	42 (22.5)	0.72 (0.42,1.25)	0.245
		Enlisted Groundcrew	72 (19.2)	125 (22.0)	0.84 (0.61,1.17)	0.306
12-19	SCL-90-R Positive Symptom Distress Index (PSDI)	All	69 (8.0)	84 (6.7)	1.20 (0.86,1.67)	0.280
		Officer	14 (4.1)	17 (3.5)	1.20 (0.58,2.47)	0.622
		Enlisted Flyer	13 (8.7)	19 (10.2)	0.84 (0.40,1.76)	0.642
		Enlisted Groundcrew	42 (11.2)	48 (8.4)	1.37 (0.88,2.12)	0.158
13-3	Uncharacterized Hepatitis	All	17 (2.0)	21 (1.7)	1.17 (0.61,2.23)	0.634
		Officer	5 (1.5)	7 (1.4)	1.03 (0.32,3.28)	0.958
		Enlisted Flyer	4 (2.6)	3 (1.6)	1.67 (0.37,7.57)	0.507
		Enlisted Groundcrew	8 (2.1)	11 (1.9)	1.11 (0.44,2.78)	0.826
13-4	Jaundice	All	12 (1.4)	35 (2.9)	0.49 (0.25,0.94)	0.025
		Officer	6 (1.8)	19 (4.0)	0.45 (0.18,1.14)	0.091
		Enlisted Flyer	3 (2.0)	1 (0.6)	3.70 (0.38,35.9)	0.260
		Enlisted Groundcrew	3 (0.8)	15 (2.7)	0.30 (0.09,1.04)	0.057

Table G-5. Summary of Unadjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal RH	Number (%) Abnormal C	Est. Relative Risk (95% C.I.)	p-Value
13-5	Chronic Liver Disease and Cirrhosis (Alcohol-related)	All	39 (4.8)	56 (4.7)	1.01 (0.67,1.54)	0.958
		Officer	15 (4.6)	14 (3.0)	1.58 (0.75,3.32)	0.229
		Enlisted Flyer	7 (5.1)	12 (6.7)	0.75 (0.29,1.95)	0.553
		Enlisted Groundcrew	17 (4.8)	30 (5.6)	0.85 (0.46,1.57)	0.602
13-6	Chronic Liver Disease and Cirrhosis (Non-alcohol-related)	All	14 (1.6)	14 (1.1)	1.44 (0.68,3.04)	0.336
		Officer	5 (1.5)	3 (0.6)	2.43 (0.58,10.18)	0.226
		Enlisted Flyer	2 (1.3)	3 (1.6)	0.82 (0.14,4.99)	0.832
		Enlisted Groundcrew	7 (1.9)	8 (1.4)	1.33 (0.48,3.69)	0.589
13-7	Liver Abscess and Sequelae of Chronic Liver Disease	All	1 (0.1)	1 (0.1)	1.44 (0.09,23.03)	0.798
		Officer	0 (0.0)	1 (0.2)	--	0.999[a]
		Enlisted Flyer	0 (0.0)	0 (0.0)	--	--
		Enlisted Groundcrew	1 (0.3)	0 (0.0)	--	0.836[a]
13-8	Enlarged Liver (Hepatomegaly)	All	14 (1.6)	27 (2.2)	0.74 (0.39,1.42)	0.361
		Officer	5 (1.5)	9 (1.8)	0.80 (0.27,2.40)	0.689
		Enlisted Flyer	6 (4.0)	3 (1.6)	2.54 (0.62,10.32)	0.193
		Enlisted Groundcrew	3 (0.8)	15 (2.6)	0.30 (0.09,1.03)	0.056
13-9	Other Liver Disorders	All	249 (28.8)	312 (25.2)	1.20 (0.99,1.46)	0.067
		Officer	93 (27.5)	121 (24.9)	1.15 (0.84,1.57)	0.399
		Enlisted Flyer	40 (26.5)	48 (25.7)	1.04 (0.64,1.70)	0.864
		Enlisted Groundcrew	116 (30.8)	143 (25.2)	1.32 (0.99,1.76)	0.062
13-10	Current Hepatomegaly	All	10 (1.2)	7 (0.6)	2.06 (0.78,5.43)	0.141
		Officer	4 (1.2)	2 (0.4)	2.90 (0.53,15.95)	0.220
		Enlisted Flyer	2 (1.3)	0 (0.0)	--	0.389[a]
		Enlisted Groundcrew	4 (1.1)	5 (0.9)	1.20 (0.32,4.51)	0.783
13-12	AST	All	63 (7.3)	82 (6.7)	1.11 (0.79,1.56)	0.552
		Officer	24 (7.1)	32 (6.5)	1.09 (0.63,1.88)	0.765
		Enlisted Flyer	10 (6.7)	16 (8.6)	0.75 (0.33,1.72)	0.501
		Enlisted Groundcrew	29 (7.9)	34 (6.1)	1.31 (0.78,2.19)	0.304
13-14	ALT	All	68 (7.9)	87 (7.1)	1.13 (0.81,1.57)	0.468
		Officer	23 (6.8)	22 (4.5)	1.54 (0.85,2.82)	0.157
		Enlisted Flyer	15 (10.0)	19 (10.3)	0.97 (0.48,1.98)	0.935
		Enlisted Groundcrew	30 (8.1)	46 (8.3)	0.98 (0.61,1.59)	0.938
13-16	GGT	All	89 (10.4)	124 (10.1)	1.03 (0.77,1.38)	0.831
		Officer	31 (9.1)	37 (7.6)	1.23 (0.75,2.02)	0.419
		Enlisted Flyer	23 (15.3)	25 (13.5)	1.16 (0.63,2.14)	0.637
		Enlisted Groundcrew	35 (9.5)	62 (11.2)	0.83 (0.54,1.29)	0.419
13-18	Alkaline Phosphatase	All	22 (2.6)	24 (1.9)	1.32 (0.74,2.37)	0.352
		Officer	4 (1.2)	12 (2.4)	0.47 (0.15,1.48)	0.200
		Enlisted Flyer	6 (4.0)	4 (2.2)	1.89 (0.52,6.81)	0.333
		Enlisted Groundcrew	12 (3.3)	8 (1.4)	2.30 (0.93,5.69)	0.071

Table G-5. Summary of Unadjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal RH	Number (%) Abnormal C	Est. Relative Risk (95% C.I.)	p-Value
13-20	Total Bilirubin	All	46 (5.4)	76 (6.2)	0.86 (0.59,1.25)	0.430
		Officer	22 (6.5)	35 (7.1)	0.90 (0.52,1.56)	0.707
		Enlisted Flyer	8 (5.3)	9 (4.9)	1.10 (0.41,2.93)	0.846
		Enlisted Groundcrew	16 (4.3)	32 (5.8)	0.74 (0.40,1.37)	0.342
13-21	Direct Bilirubin	All	1 (0.1)	5 (0.4)	0.29 (0.03,2.45)	0.196
		Officer	1 (0.3)	3 (0.6)	0.48 (0.05,4.62)	0.524
		Enlisted Flyer	0 (0.0)	0 (0.0)	--	--
		Enlisted Groundcrew	0 (0.0)	2 (0.4)	--	0.667[a]
13-23	Lactic Dehydrogenase	All	81 (9.4)	129 (10.5)	0.89 (0.66,1.19)	0.424
		Officer	32 (9.4)	53 (10.8)	0.85 (0.54,1.36)	0.506
		Enlisted Flyer	13 (8.7)	15 (8.2)	1.07 (0.49,2.32)	0.866
		Enlisted Groundcrew	36 (9.8)	61 (11.0)	0.88 (0.57,1.35)	0.555
13-25	Cholesterol	All	130 (15.1)	182 (14.8)	1.03 (0.81,1.31)	0.826
		Officer	39 (11.5)	68 (13.9)	0.80 (0.53,1.22)	0.310
		Enlisted Flyer	22 (14.7)	28 (15.1)	0.96 (0.53,1.77)	0.905
		Enlisted Groundcrew	69 (18.7)	86 (15.5)	1.26 (0.89,1.78)	0.198
13-27	HDL Cholesterol	All	71 (8.3)	90 (7.3)	1.14 (0.83,1.58)	0.421
		Officer	19 (5.6)	24 (4.9)	1.15 (0.62,2.13)	0.664
		Enlisted Flyer	16 (10.7)	18 (9.7)	1.12 (0.55,2.27)	0.762
		Enlisted Groundcrew	36 (9.8)	48 (8.7)	1.14 (0.73,1.80)	0.561
13-29	Cholesterol-HDL Ratio	All	356 (41.5)	505 (41.1)	1.02 (0.85,1.22)	0.843
		Officer	114 (33.5)	156 (31.9)	1.08 (0.80,1.45)	0.623
		Enlisted Flyer	58 (38.9)	87 (47.0)	0.72 (0.46,1.11)	0.138
		Enlisted Groundcrew	184 (49.9)	262 (47.1)	1.12 (0.86,1.45)	0.414
13-31	Triglycerides	All	188 (21.9)	250 (20.3)	1.10 (0.89,1.36)	0.377
		Officer	60 (17.7)	82 (16.7)	1.07 (0.74,1.54)	0.717
		Enlisted Flyer	30 (20.0)	51 (27.6)	0.66 (0.39,1.10)	0.109
		Enlisted Groundcrew	98 (26.6)	117 (21.0)	1.36 (1.00,1.85)	0.052
13-33	Creatine Phosphokinase	All	72 (8.4)	115 (9.3)	0.89 (0.65,1.21)	0.448
		Officer	26 (7.6)	44 (9.0)	0.84 (0.51,1.39)	0.497
		Enlisted Flyer	7 (4.7)	15 (8.1)	0.55 (0.22,1.40)	0.212
		Enlisted Groundcrew	39 (10.6)	56 (10.1)	1.06 (0.69,1.62)	0.807
13-35	Serum Amylase	All	25 (2.9)	38 (3.1)	0.94 (0.56,1.57)	0.816
		Officer	7 (2.1)	22 (4.5)	0.45 (0.19,1.06)	0.067
		Enlisted Flyer	4 (2.7)	3 (1.6)	1.66 (0.37,7.54)	0.510
		Enlisted Groundcrew	14 (3.8)	13 (2.3)	1.65 (0.77,3.55)	0.202
13-36	Antibodies for Hepatitis A	All	283 (32.5)	421 (33.7)	0.95 (0.79,1.14)	0.580
		Officer	92 (27.0)	133 (27.0)	1.00 (0.73,1.36)	0.999
		Enlisted Flyer	74 (49.0)	86 (46.0)	1.13 (0.73,1.73)	0.581
		Enlisted Groundcrew	117 (31.0)	202 (35.4)	0.82 (0.62,1.08)	0.153

Table G-5. Summary of Unadjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal RH	Number (%) Abnormal C	Est. Relative Risk (95% C.I.)	p-Value
13-37	Prior Hepatitis B	All	77 (8.9)	170 (13.6)	0.62 (0.46,0.82)	0.001
		Officer	13 (3.8)	37 (7.5)	0.49 (0.26,0.94)	0.031
		Enlisted Flyer	19 (12.6)	37 (19.8)	0.58 (0.32,1.06)	0.079
		Enlisted Groundcrew	45 (11.9)	96 (16.9)	0.66 (0.45,0.97)	0.035
13-38	Current Hepatitis B	All	1 (0.1)	2 (0.2)	0.72 (0.07,7.94)	0.784
		Officer	0 (0.0)	0 (0.0)	--	--
		Enlisted Flyer	0 (0.0)	0 (0.0)	--	--
		Enlisted Groundcrew	1 (0.3)	2 (0.4)	0.75 (0.07,8.34)	0.817
13-39	Antibodies for Hepatitis C	All	9 (1.0)	18 (1.4)	0.72 (0.32,1.60)	0.408
		Officer	1 (0.3)	4 (0.8)	0.36 (0.04,3.24)	0.362
		Enlisted Flyer	1 (0.7)	2 (1.1)	0.62 (0.06,6.87)	0.694
		Enlisted Groundcrew	7 (1.9)	12 (2.1)	0.88 (0.34,2.25)	0.785
13-40	Stool Hemoccult	All	29 (3.5)	53 (4.4)	0.78 (0.49,1.23)	0.279
		Officer	14 (4.2)	22 (4.6)	0.92 (0.46,1.83)	0.818
		Enlisted Flyer	2 (1.4)	7 (3.9)	0.34 (0.07,1.65)	0.179
		Enlisted Groundcrew	13 (3.7)	24 (4.5)	0.81 (0.41,1.61)	0.547
13-42	Prealbumin	All	13 (1.5)	11 (0.9)	1.70 (0.76,3.82)	0.195
		Officer	5 (1.5)	7 (1.4)	1.03 (0.32,3.27)	0.960
		Enlisted Flyer	1 (0.7)	1 (0.5)	1.23 (0.08,19.91)	0.882
		Enlisted Groundcrew	7 (1.9)	3 (0.5)	3.56 (0.92,13.87)	0.067
13-44	Albumin	All	3 (0.3)	10 (0.8)	0.43 (0.12,1.56)	0.170
		Officer	3 (0.9)	4 (0.8)	1.08 (0.24,4.86)	0.919
		Enlisted Flyer	0 (0.0)	1 (0.5)	--	0.999[a]
		Enlisted Groundcrew	0 (0.0)	5 (0.9)	--	0.171[a]
13-46	α-1-Acid Glycoprotein	All	37 (4.3)	40 (3.2)	1.34 (0.85,2.11)	0.209
		Officer	8 (2.4)	15 (3.1)	0.76 (0.32,1.82)	0.542
		Enlisted Flyer	9 (6.0)	7 (3.8)	1.62 (0.59,4.47)	0.348
		Enlisted Groundcrew	20 (5.4)	18 (3.2)	1.71 (0.89,3.28)	0.105
13-50	α-2-Macroglobulin	All	24 (2.8)	47 (3.8)	0.72 (0.44,1.19)	0.199
		Officer	8 (2.4)	18 (3.7)	0.63 (0.27,1.47)	0.287
		Enlisted Flyer	5 (3.3)	11 (5.9)	0.55 (0.19,1.61)	0.271
		Enlisted Groundcrew	11 (3.0)	18 (3.2)	0.92 (0.43,1.97)	0.827
13-52	Apolipoprotein B	All	423 (49.2)	653 (53.0)	0.86 (0.72,1.02)	0.087
		Officer	149 (43.8)	242 (49.4)	0.80 (0.61,1.06)	0.114
		Enlisted Flyer	72 (48.0)	116 (62.7)	0.55 (0.35,0.85)	0.007
		Enlisted Groundcrew	202 (54.7)	295 (53.1)	1.07 (0.82,1.39)	0.615
13-54	C3 Complement	All	15 (1.7)	28 (2.3)	0.76 (0.41,1.44)	0.398
		Officer	6 (1.8)	14 (2.9)	0.61 (0.23,1.61)	0.317
		Enlisted Flyer	1 (0.7)	5 (2.7)	0.24 (0.03,2.09)	0.197
		Enlisted Groundcrew	8 (2.2)	9 (1.6)	1.35 (0.51,3.52)	0.544

Table G-5. Summary of Unadjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal RH	Number (%) Abnormal C	Est. Relative Risk (95% C.I.)	p-Value
13-56	C4 Complement	All	2 (0.2)	2 (0.2)	1.43 (0.20,10.20)	0.719
		Officer	2 (0.6)	1 (0.2)	2.89 (0.26,32.04)	0.386
		Enlisted Flyer	0 (0.0)	1 (0.5)	--	0.999[a]
		Enlisted Groundcrew	0 (0.0)	0 (0.0)	--	--
13-58	Haptoglobin	All	281 (32.7)	343 (27.9)	1.26 (1.04,1.52)	0.017
		Officer	84 (24.7)	106 (21.6)	1.19 (0.86,1.65)	0.300
		Enlisted Flyer	59 (39.3)	62 (33.5)	1.29 (0.82,2.01)	0.271
		Enlisted Groundcrew	138 (37.4)	175 (31.5)	1.30 (0.99,1.72)	0.063
13-60	Transferrin	All	70 (8.1)	134 (10.9)	0.73 (0.54,0.98)	0.036
		Officer	24 (7.1)	52 (10.6)	0.64 (0.39,1.06)	0.083
		Enlisted Flyer	15 (10.0)	21 (11.4)	0.87 (0.43,1.75)	0.691
		Enlisted Groundcrew	31 (8.4)	61 (11.0)	0.74 (0.47,1.17)	0.202
14-3	Essential Hypertension	All	345 (40.6)	509 (41.7)	0.95 (0.80,1.14)	0.606
		Officer	128 (38.9)	199 (41.5)	0.90 (0.68,1.20)	0.467
		Enlisted Flyer	71 (47.7)	80 (43.5)	1.18 (0.77,1.83)	0.447
		Enlisted Groundcrew	146 (39.2)	230 (41.4)	0.92 (0.70,1.20)	0.519
14-4	Heart Disease (Excluding Essential Hypertension)	All	568 (66.1)	749 (60.8)	1.26 (1.05,1.51)	0.013
		Officer	238 (71.3)	324 (66.9)	1.22 (0.90,1.66)	0.191
		Enlisted Flyer	112 (75.2)	111 (59.7)	2.05 (1.27,3.28)	0.003
		Enlisted Groundcrew	218 (58.0)	314 (55.9)	1.09 (0.84,1.42)	0.523
14-5	Myocardial Infarction	All	74 (8.6)	102 (8.3)	1.04 (0.76,1.43)	0.786
		Officer	28 (8.4)	42 (8.7)	0.96 (0.58,1.59)	0.882
		Enlisted Flyer	16 (10.7)	15 (8.1)	1.37 (0.65,2.87)	0.403
		Enlisted Groundcrew	30 (8.0)	45 (8.0)	1.00 (0.62,1.61)	0.987
14-6	Stroke or Transient Ischemia Attack	All	11 (1.3)	14 (1.1)	1.13 (0.51,2.50)	0.766
		Officer	5 (1.5)	5 (1.0)	1.46 (0.42,5.07)	0.555
		Enlisted Flyer	0 (0.0)	3 (1.6)	--	0.330[a]
		Enlisted Groundcrew	6 (1.6)	6 (1.1)	1.50 (0.48,4.69)	0.483
14-8	Systolic Blood Pressure	All	181 (21.1)	262 (21.3)	0.99 (0.80,1.22)	0.914
		Officer	78 (23.4)	112 (23.1)	1.01 (0.73,1.41)	0.944
		Enlisted Flyer	36 (24.2)	43 (23.1)	1.06 (0.64,1.76)	0.823
		Enlisted Groundcrew	67 (17.8)	107 (19.0)	0.92 (0.66,1.29)	0.638
14-10	Diastolic Blood Pressure	All	45 (5.2)	61 (5.0)	1.06 (0.71,1.58)	0.769
		Officer	20 (6.0)	22 (4.5)	1.34 (0.72,2.49)	0.360
		Enlisted Flyer	8 (5.4)	8 (4.3)	1.26 (0.46,3.45)	0.649
		Enlisted Groundcrew	17 (4.5)	31 (5.5)	0.81 (0.44,1.49)	0.499
14-11	Heart Sounds	All	31 (3.6)	62 (5.0)	0.71 (0.45,1.10)	0.116
		Officer	11 (3.3)	26 (5.4)	0.60 (0.29,1.23)	0.164
		Enlisted Flyer	7 (4.7)	11 (5.9)	0.78 (0.30,2.08)	0.625
		Enlisted Groundcrew	13 (3.5)	25 (4.4)	0.77 (0.39,1.52)	0.452

Table G-5. Summary of Unadjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal RH	Number (%) Abnormal C	Est. Relative Risk (95% C.I.)	p-Value
14-12	Overall Electrocardiograph	All	268 (31.2)	384 (31.2)	1.00 (0.83,1.21)	0.988
		Officer	120 (35.9)	163 (33.7)	1.10 (0.82,1.48)	0.506
		Enlisted Flyer	60 (40.3)	62 (33.3)	1.35 (0.86,2.11)	0.190
		Enlisted Groundcrew	88 (23.4)	159 (28.3)	0.77 (0.57,1.05)	0.096
14-13	Right Bundle Branch Block	All	21 (2.4)	33 (2.7)	0.91 (0.52,1.58)	0.739
		Officer	8 (2.4)	13 (2.7)	0.89 (0.36,2.17)	0.796
		Enlisted Flyer	8 (5.4)	7 (3.8)	1.45 (0.51,4.10)	0.482
		Enlisted Groundcrew	5 (1.3)	13 (2.3)	0.57 (0.20,1.61)	0.288
14-14	Left Bundle Branch Block	All	5 (0.6)	12 (1.0)	0.60 (0.21,1.70)	0.317
		Officer	2 (0.6)	6 (1.2)	0.48 (0.10,2.39)	0.370
		Enlisted Flyer	1 (0.7)	0 (0.0)	--	0.911[a]
		Enlisted Groundcrew	2 (0.5)	6 (1.1)	0.50 (0.10,2.47)	0.391
14-15	Non-Specific ST- and T-Wave Changes	All	160 (18.6)	222 (18.0)	1.04 (0.83,1.30)	0.724
		Officer	70 (21.0)	95 (19.6)	1.09 (0.77,1.53)	0.641
		Enlisted Flyer	33 (22.1)	34 (18.3)	1.27 (0.74,2.17)	0.380
		Enlisted Groundcrew	57 (15.2)	93 (16.5)	0.90 (0.63,1.29)	0.570
14-16	Bradycardia	All	24 (2.8)	49 (4.0)	0.69 (0.42,1.14)	0.142
		Officer	15 (4.5)	31 (6.4)	0.69 (0.36,1.29)	0.245
		Enlisted Flyer	5 (3.4)	5 (2.7)	1.26 (0.36,4.43)	0.722
		Enlisted Groundcrew	4 (1.1)	13 (2.3)	0.45 (0.15,1.40)	0.170
14-17	Tachycardia	All	6 (0.7)	4 (0.3)	2.16 (0.61,7.68)	0.228
		Officer	1 (0.3)	1 (0.2)	1.45 (0.09,23.27)	0.793
		Enlisted Flyer	3 (2.0)	0 (0.0)	--	0.174[a]
		Enlisted Groundcrew	2 (0.5)	3 (0.5)	1.00 (0.17,5.99)	0.997
14-18	Arrhythmia	All	51 (5.9)	68 (5.5)	1.08 (0.74,1.57)	0.686
		Officer	25 (7.5)	25 (5.2)	1.49 (0.84,2.63)	0.176
		Enlisted Flyer	13 (8.7)	12 (6.5)	1.39 (0.61,3.13)	0.433
		Enlisted Groundcrew	13 (3.5)	31 (5.5)	0.61 (0.32,1.19)	0.147
14-19	Evidence of Prior Myocardial Infarction	All	34 (4.0)	53 (4.3)	0.92 (0.59,1.42)	0.698
		Officer	15 (4.5)	23 (4.8)	0.94 (0.48,1.83)	0.862
		Enlisted Flyer	7 (4.7)	9 (4.8)	0.97 (0.35,2.67)	0.952
		Enlisted Groundcrew	12 (3.2)	21 (3.7)	0.85 (0.41,1.75)	0.657
14-20	ECG: Other Diagnoses	All	3 (0.3)	1 (0.1)	4.31 (0.45,41.55)	0.168
		Officer	1 (0.3)	0 (0.0)	--	0.852[a]
		Enlisted Flyer	0 (0.0)	0 (0.0)	--	--
		Enlisted Groundcrew	2 (0.5)	1 (0.2)	3.00 (0.27,33.20)	0.370
14-21	Funduscopic Examination	All	105 (12.2)	156 (12.7)	0.96 (0.74,1.25)	0.767
		Officer	42 (12.6)	49 (10.1)	1.28 (0.83,1.99)	0.267
		Enlisted Flyer	30 (20.1)	32 (17.3)	1.21 (0.69,2.09)	0.508
		Enlisted Groundcrew	33 (8.8)	75 (13.3)	0.62 (0.41,0.96)	0.033

Table G-5. Summary of Unadjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal RH	Number (%) Abnormal C	Est. Relative Risk (95% C.I.)	p-Value
14-22	Carotid Bruits	All	23 (2.7)	33 (2.7)	1.00 (0.58,1.71)	0.999
		Officer	6 (1.8)	12 (2.5)	0.72 (0.27,1.94)	0.515
		Enlisted Flyer	8 (5.4)	5 (2.7)	2.05 (0.66,6.41)	0.215
		Enlisted Groundcrew	9 (2.4)	16 (2.8)	0.84 (0.37,1.91)	0.673
14-23	Radial Pulses	All	7 (0.8)	4 (0.3)	2.52 (0.74,8.64)	0.131
		Officer	2 (0.6)	2 (0.4)	1.45 (0.20,10.36)	0.710
		Enlisted Flyer	0 (0.0)	0 (0.0)	--	--
		Enlisted Groundcrew	5 (1.3)	2 (0.4)	3.77 (0.73,19.55)	0.114
14-24	Femoral Pulses	All	19 (2.2)	15 (1.2)	1.83 (0.93,3.63)	0.080
		Officer	7 (2.1)	8 (1.7)	1.27 (0.46,3.55)	0.643
		Enlisted Flyer	5 (3.4)	3 (1.6)	2.11 (0.50,8.96)	0.313
		Enlisted Groundcrew	7 (1.9)	4 (0.7)	2.65 (0.77,9.10)	0.123
14-25	Popliteal Pulses	All	23 (2.7)	28 (2.3)	1.18 (0.68,2.06)	0.561
		Officer	7 (2.1)	12 (2.5)	0.84 (0.33,2.16)	0.717
		Enlisted Flyer	5 (3.4)	4 (2.2)	1.57 (0.41,5.96)	0.506
		Enlisted Groundcrew	11 (2.9)	12 (2.1)	1.38 (0.60,3.16)	0.445
14-26	Dorsalis Pedis Pulses	All	69 (8.0)	95 (7.7)	1.04 (0.76,1.44)	0.796
		Officer	27 (8.1)	32 (6.6)	1.24 (0.73,2.11)	0.429
		Enlisted Flyer	18 (12.1)	17 (9.2)	1.36 (0.67,2.74)	0.392
		Enlisted Groundcrew	24 (6.4)	46 (8.2)	0.76 (0.46,1.28)	0.305
14-27	Posterior Tibial Pulses	All	58 (6.8)	64 (5.2)	1.32 (0.91,1.90)	0.142
		Officer	22 (6.6)	23 (4.8)	1.41 (0.77,2.57)	0.263
		Enlisted Flyer	14 (9.4)	13 (7.1)	1.36 (0.62,2.98)	0.449
		Enlisted Groundcrew	22 (5.9)	28 (5.0)	1.19 (0.67,2.10)	0.562
14-28	Leg Pulses	All	94 (10.9)	123 (10.0)	1.10 (0.83,1.47)	0.496
		Officer	36 (10.8)	40 (8.3)	1.34 (0.83,2.15)	0.228
		Enlisted Flyer	25 (16.8)	22 (12.0)	1.48 (0.79,2.74)	0.218
		Enlisted Groundcrew	33 (8.8)	61 (10.9)	0.79 (0.51,1.23)	0.300
14-29	Peripheral Pulses	All	97 (11.3)	126 (10.3)	1.11 (0.84,1.47)	0.454
		Officer	37 (11.1)	42 (8.7)	1.31 (0.82,2.08)	0.258
		Enlisted Flyer	25 (16.8)	22 (12.0)	1.48 (0.79,2.74)	0.218
		Enlisted Groundcrew	35 (9.3)	62 (11.0)	0.83 (0.53,1.28)	0.396
14-30	ICVI Index	All	33 (3.8)	45 (3.7)	1.06 (0.67,1.67)	0.819
		Officer	13 (3.9)	15 (3.1)	1.27 (0.59,2.70)	0.541
		Enlisted Flyer	7 (4.7)	12 (6.5)	0.71 (0.27,1.86)	0.492
		Enlisted Groundcrew	13 (3.5)	18 (3.2)	1.09 (0.53,2.24)	0.825
15-14	Prothrombin Time	All	10 (1.5)	13 (1.3)	1.14 (0.50,2.61)	0.761
		Officer	6 (2.3)	7 (1.7)	1.31 (0.43,3.93)	0.634
		Enlisted Flyer	0 (0.0)	1 (0.6)	--	0.999[a]
		Enlisted Groundcrew	4 (1.3)	5 (1.1)	1.19 (0.32,4.45)	0.801

Table G-5. Summary of Unadjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal RH	Number (%) Abnormal C	Est. Relative Risk (95% C.I.)	p-Value
15-15	RBC Morphology	All	64 (7.4)	79 (6.3)	1.18 (0.84,1.66)	0.339
		Officer	20 (5.9)	28 (5.7)	1.03 (0.57,1.87)	0.910
		Enlisted Flyer	15 (9.9)	17 (9.1)	1.10 (0.53,2.29)	0.793
		Enlisted Groundcrew	29 (7.8)	34 (6.0)	1.32 (0.79,2.21)	0.286
15-18	Absolute Neutrophils (bands) (Zero vs. Nonzero)	All	146 (16.9)	212 (17.0)	0.99 (0.79,1.25)	0.945
		Officer	47 (13.8)	87 (17.7)	0.75 (0.51,1.10)	0.136
		Enlisted Flyer	36 (23.8)	27 (14.4)	1.86 (1.07,3.23)	0.029
		Enlisted Groundcrew	63 (16.8)	98 (17.2)	0.97 (0.69,1.38)	0.880
15-22	Absolute Eosinophils (Zero vs. Nonzero)	All	106 (12.2)	153 (12.3)	1.00 (0.77,1.30)	0.995
		Officer	36 (10.6)	45 (9.1)	1.18 (0.74,1.86)	0.493
		Enlisted Flyer	17 (11.3)	22 (11.8)	0.95 (0.49,1.86)	0.885
		Enlisted Groundcrew	53 (14.2)	86 (15.1)	0.93 (0.64,1.34)	0.689
15-24	Absolute Basophils (Zero vs. Nonzero)	All	493 (56.9)	669 (53.6)	1.15 (0.96,1.36)	0.126
		Officer	192 (56.3)	261 (52.9)	1.15 (0.87,1.51)	0.338
		Enlisted Flyer	76 (50.3)	100 (53.5)	0.88 (0.57,1.35)	0.565
		Enlisted Groundcrew	225 (60.2)	308 (54.1)	1.28 (0.98,1.67)	0.068
16-3	Past Thyroid Disease	All	65 (7.5)	105 (8.4)	0.89 (0.64,1.22)	0.456
		Officer	29 (8.6)	46 (9.3)	0.91 (0.56,1.48)	0.704
		Enlisted Flyer	15 (10.0)	14 (7.5)	1.37 (0.64,2.94)	0.415
		Enlisted Groundcrew	21 (5.6)	45 (7.9)	0.69 (0.40,1.18)	0.171
16-4	Composite Diabetes Indicator	All	145 (16.9)	209 (17.0)	0.99 (0.79,1.25)	0.960
		Officer	52 (15.4)	71 (14.5)	1.08 (0.73,1.59)	0.709
		Enlisted Flyer	27 (18.2)	38 (20.7)	0.86 (0.50,1.48)	0.583
		Enlisted Groundcrew	66 (17.6)	100 (17.9)	0.98 (0.70,1.38)	0.915
16-7	Thyroid Gland	All	6 (0.7)	16 (1.3)	0.53 (0.21,1.36)	0.171
		Officer	4 (1.2)	11 (2.3)	0.52 (0.16,1.63)	0.260
		Enlisted Flyer	1 (0.7)	1 (0.5)	1.27 (0.08,20.41)	0.868
		Enlisted Groundcrew	1 (0.3)	4 (0.7)	0.37 (0.04,3.32)	0.374
16-8	Testicular Examination	All	39 (4.5)	47 (3.8)	1.20 (0.78,1.85)	0.409
		Officer	16 (4.8)	27 (5.5)	0.86 (0.45,1.62)	0.635
		Enlisted Flyer	9 (6.1)	8 (4.3)	1.42 (0.54,3.79)	0.478
		Enlisted Groundcrew	14 (3.7)	12 (2.1)	1.77 (0.81,3.87)	0.152
16-12	Thyroxine	All	23 (2.7)	32 (2.7)	1.03 (0.60,1.77)	0.928
		Officer	13 (4.0)	16 (3.4)	1.17 (0.56,2.47)	0.674
		Enlisted Flyer	3 (2.1)	3 (1.6)	1.27 (0.25,6.39)	0.772
		Enlisted Groundcrew	7 (1.9)	13 (2.4)	0.79 (0.31,2.01)	0.624
16-13	Anti-Thyroid Antibodies	All	5 (0.6)	7 (0.6)	1.02 (0.32,3.22)	0.975
		Officer	2 (0.6)	4 (0.9)	0.72 (0.13,3.93)	0.701
		Enlisted Flyer	2 (1.4)	1 (0.5)	2.55 (0.23,28.40)	0.447
		Enlisted Groundcrew	1 (0.3)	2 (0.4)	0.74 (0.07,8.18)	0.805

Table G-5. Summary of Unadjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal RH	Number (%) Abnormal C	Est. Relative Risk (95% C.I.)	p-Value
16-15	Fasting Glucose	All	152 (17.5)	212 (17.0)	1.04 (0.83,1.31)	0.741
		Officer	56 (16.5)	75 (15.2)	1.11 (0.76,1.61)	0.603
		Enlisted Flyer	29 (19.2)	36 (19.3)	1.00 (0.58,1.72)	0.991
		Enlisted Groundcrew	67 (17.7)	101 (17.8)	1.00 (0.71,1.40)	0.992
16-17	2-Hour Postprandial Glucose	All	113 (15.8)	161 (15.7)	1.01 (0.77,1.31)	0.960
		Officer	52 (18.2)	54 (12.9)	1.51 (1.00,2.28)	0.052
		Enlisted Flyer	22 (18.2)	31 (21.2)	0.82 (0.45,1.52)	0.534
		Enlisted Groundcrew	39 (12.7)	76 (16.6)	0.73 (0.48,1.11)	0.136
16-18	Fasting Urinary Glucose	All	35 (4.0)	54 (4.3)	0.93 (0.60,1.44)	0.745
		Officer	11 (3.2)	12 (2.4)	1.35 (0.59,3.09)	0.482
		Enlisted Flyer	8 (5.3)	9 (4.8)	1.11 (0.42,2.94)	0.839
		Enlisted Groundcrew	16 (4.2)	33 (5.8)	0.72 (0.39,1.32)	0.288
16-19	2-Hour Postprandial Urinary Glucose	All	179 (25.1)	224 (21.9)	1.19 (0.95,1.50)	0.122
		Officer	68 (24.0)	73 (17.5)	1.49 (1.03,2.17)	0.034
		Enlisted Flyer	28 (23.1)	43 (29.7)	0.71 (0.41,1.24)	0.233
		Enlisted Groundcrew	83 (26.9)	108 (23.6)	1.20 (0.86,1.67)	0.291
16-23	α-1-C Hemoglobin	All	97 (11.2)	130 (10.4)	1.08 (0.82,1.43)	0.571
		Officer	28 (8.3)	37 (7.5)	1.11 (0.67,1.85)	0.684
		Enlisted Flyer	17 (11.3)	29 (15.5)	0.69 (0.36,1.31)	0.259
		Enlisted Groundcrew	52 (13.8)	64 (11.2)	1.26 (0.85,1.86)	0.250
16-25	Total Testosterone	All	72 (8.5)	90 (7.3)	1.17 (0.85,1.61)	0.344
		Officer	29 (8.8)	34 (7.0)	1.28 (0.76,2.14)	0.352
		Enlisted Flyer	12 (8.2)	11 (6.0)	1.39 (0.60,3.25)	0.445
		Enlisted Groundcrew	31 (8.3)	45 (8.0)	1.03 (0.64,1.67)	0.890
16-27	Free Testosterone	All	15 (1.8)	20 (1.6)	1.08 (0.55,2.13)	0.815
		Officer	7 (2.1)	10 (2.1)	1.03 (0.39,2.73)	0.954
		Enlisted Flyer	6 (4.1)	1 (0.5)	7.76 (0.92,65.18)	0.059
		Enlisted Groundcrew	2 (0.5)	9 (1.6)	0.33 (0.07,1.53)	0.157
16-29	Estradiol	All	236 (27.1)	350 (28.0)	0.96 (0.79,1.16)	0.666
		Officer	80 (23.5)	139 (28.1)	0.78 (0.57,1.08)	0.131
		Enlisted Flyer	44 (29.1)	59 (31.6)	0.89 (0.56,1.42)	0.632
		Enlisted Groundcrew	112 (29.6)	152 (26.7)	1.16 (0.87,1.55)	0.319
16-31	LH	All	49 (5.6)	70 (5.6)	1.01 (0.69,1.47)	0.971
		Officer	24 (7.0)	28 (5.7)	1.26 (0.72,2.21)	0.422
		Enlisted Flyer	6 (4.0)	8 (4.3)	0.93 (0.31,2.73)	0.889
		Enlisted Groundcrew	19 (5.0)	34 (6.0)	0.83 (0.47,1.49)	0.538
16-33	FSH	All	72 (8.3)	98 (7.8)	1.06 (0.77,1.46)	0.713
		Officer	39 (11.4)	48 (9.7)	1.20 (0.77,1.88)	0.424
		Enlisted Flyer	17 (11.3)	14 (7.5)	1.57 (0.75,3.29)	0.235
		Enlisted Groundcrew	16 (4.2)	36 (6.3)	0.66 (0.36,1.20)	0.171

Table G-5. Summary of Unadjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal RH	Number (%) Abnormal C	Est. Relative Risk (95% C.I.)	p-Value
17-14	ANA Test	All	432 (52.1)	624 (52.0)	1.00 (0.84,1.19)	0.998
		Officer	168 (51.4)	251 (52.8)	0.94 (0.71,1.25)	0.683
		Enlisted Flyer	73 (51.4)	87 (48.9)	1.11 (0.71,1.72)	0.653
		Enlisted Groundcrew	191 (52.9)	286 (52.4)	1.02 (0.78,1.33)	0.876
17-15	ANA Thyroid Microsomal Antibody	All	24 (2.9)	34 (2.8)	1.02 (0.60,1.73)	0.941
		Officer	11 (3.4)	14 (3.0)	1.15 (0.51,2.56)	0.739
		Enlisted Flyer	3 (2.1)	5 (2.8)	0.75 (0.18,3.18)	0.693
		Enlisted Groundcrew	10 (2.8)	15 (2.8)	1.01 (0.45,2.27)	0.984
17-16	MSK Smooth Muscle Antibody	All	101 (12.2)	145 (12.1)	1.01 (0.77,1.32)	0.959
		Officer	43 (13.2)	49 (10.3)	1.32 (0.85,2.04)	0.217
		Enlisted Flyer	12 (8.5)	29 (16.3)	0.47 (0.23,0.97)	0.040
		Enlisted Groundcrew	46 (12.7)	67 (12.3)	1.04 (0.70,1.56)	0.833
17-17	MSK Mitochondrial Antibody	All	4 (0.5)	2 (0.2)	2.90 (0.53,15.86)	0.203
		Officer	4 (1.2)	1 (0.2)	5.87 (0.65,52.76)	0.114
		Enlisted Flyer	0 (0.0)	1 (0.6)	--	0.999[a]
		Enlisted Groundcrew	0 (0.0)	0 (0.0)	--	--
17-18	MSK Parietal Antibody	All	36 (4.3)	51 (4.3)	1.02 (0.66,1.58)	0.927
		Officer	14 (4.3)	15 (3.2)	1.37 (0.65,2.88)	0.404
		Enlisted Flyer	5 (3.5)	10 (5.6)	0.61 (0.20,1.84)	0.382
		Enlisted Groundcrew	17 (4.7)	26 (4.8)	0.99 (0.53,1.85)	0.971
17-19	Rheumatoid Factor	All	89 (10.7)	134 (11.2)	0.95 (0.72,1.27)	0.748
		Officer	43 (13.2)	56 (11.8)	1.13 (0.74,1.73)	0.565
		Enlisted Flyer	19 (13.4)	23 (12.9)	1.04 (0.54,2.00)	0.904
		Enlisted Groundcrew	27 (7.5)	55 (10.1)	0.72 (0.45,1.17)	0.184
18-3	Asthma	All	41 (4.8)	44 (3.5)	1.37 (0.89,2.11)	0.158
		Officer	18 (5.3)	17 (3.5)	1.57 (0.80,3.10)	0.191
		Enlisted Flyer	3 (2.0)	8 (4.3)	0.46 (0.12,1.76)	0.257
		Enlisted Groundcrew	20 (5.4)	19 (3.4)	1.64 (0.86,3.11)	0.132
18-4	Bronchitis	All	183 (21.6)	235 (19.2)	1.16 (0.94,1.44)	0.177
		Officer	60 (18.2)	86 (17.8)	1.03 (0.71,1.48)	0.886
		Enlisted Flyer	40 (27.8)	35 (19.1)	1.63 (0.97,2.73)	0.066
		Enlisted Groundcrew	83 (22.3)	114 (20.4)	1.12 (0.81,1.54)	0.496
18-5	Pneumonia	All	85 (10.3)	140 (11.6)	0.87 (0.66,1.16)	0.344
		Officer	34 (10.6)	64 (13.6)	0.75 (0.48,1.17)	0.200
		Enlisted Flyer	19 (13.7)	15 (8.3)	1.74 (0.85,3.57)	0.129
		Enlisted Groundcrew	32 (8.8)	61 (11.0)	0.78 (0.50,1.22)	0.271
18-6	Thorax and Lung Abnormalities	All	102 (11.7)	140 (11.2)	1.05 (0.80,1.38)	0.704
		Officer	31 (9.1)	33 (6.7)	1.40 (0.84,2.33)	0.200
		Enlisted Flyer	29 (19.2)	34 (18.2)	1.07 (0.62,1.85)	0.810
		Enlisted Groundcrew	42 (11.1)	73 (12.8)	0.85 (0.57,1.27)	0.434

Table G-5. Summary of Unadjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal RH	Number (%) Abnormal C	Est. Relative Risk (95% C.I.)	p-Value
18-7	X-ray Interpretation	All	98 (11.3)	118 (9.4)	1.22 (0.92,1.62)	0.166
		Officer	39 (11.4)	42 (8.5)	1.39 (0.88,2.20)	0.160
		Enlisted Flyer	16 (10.6)	17 (9.1)	1.19 (0.58,2.43)	0.643
		Enlisted Groundcrew	43 (11.4)	59 (10.4)	1.12 (0.74,1.70)	0.599

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with abnormalities.

--: Relative risk, confidence interval, and p-value are not presented because of the sparse number of participants with abnormalities.

Note: RH = Ranch Hand; C = Comparison.

Table G-6. Summary of Unadjusted Results for Dichotomous Variables – Model 2 (Ranch Hands: Log_2 (Initial Dioxin))

Table Ref.	Clinical Parameter	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
9-3	Self-perception of Health	1.02 (0.85,1.21)	0.859
9-4	Appearance of Illness or Distress	0.71 (0.42,1.20)	0.178
9-5	Relative Age Appearance	1.05 (0.84,1.30)	0.694
9-7	Body Fat	1.00 (0.87,1.15)	0.989
9-9	Erythrocyte Sedimentation Rate	1.17 (0.93,1.46)	0.179
10-3	Skin Neoplasms	0.78 (0.67,0.91)	0.001
10-4	Malignant Skin Neoplasms	0.79 (0.64,0.96)	0.015
10-5	Benign Skin Neoplasms	0.82 (0.69,0.98)	0.022
10-6	Skin Neoplasms of Uncertain Behavior or Unspecified Nature	0.87 (0.44,1.75)	0.696
10-7	Basal Cell Carcinoma (All Sites Combined)	0.67 (0.53,0.85)	<0.001
10-8	Basal Cell Carcinoma (Ear, Face, Head, and Neck)	0.63 (0.48,0.83)	<0.001
10-9	Basal Cell Carcinoma (Trunk)	0.79 (0.56,1.13)	0.184
10-10	Basal Cell Carcinoma (Upper Extremities)	0.51 (0.26,0.99)	0.024
10-11	Basal Cell Carcinoma (Lower Extremities)	1.09 (0.39,3.02)	0.867
10-12	Squamous Cell Carcinoma	0.95 (0.58,1.55)	0.821
10-13	Nonmelanoma	0.73 (0.59,0.90)	0.003
10-14	Melanoma	1.12 (0.69,1.80)	0.660
10-15	Systemic Neoplasms (All Sites Combined)	0.93 (0.80,1.07)	0.308
10-16	Malignant Systemic Neoplasms	0.62 (0.46,0.84)	0.001
10-17	Benign Systemic Neoplasms	1.03 (0.88,1.20)	0.718
10-18	Systemic Neoplasms of Uncertain Behavior or Unspecified Nature	0.84 (0.49,1.47)	0.534
10-19	Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck)	0.50 (0.20,1.23)	0.081
10-20	Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx)	0.97 (0.39,2.41)	0.953
10-21	Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum)	--	--
10-22	Malignant Systemic Neoplasms (Thyroid Gland)	0.12 (0.01,2.59)	0.046
10-23	Malignant Systemic Neoplasms (Bronchus and Lung)	0.46 (0.20,1.04)	0.030
10-24	Malignant Systemic Neoplasms (Liver)	1.76 (0.73,4.22)	0.231
10-25	Malignant Systemic Neoplasms (Colon and Rectum)	0.76 (0.39,1.49)	0.405
10-26	Malignant Systemic Neoplasms (Kidney and Bladder)	0.72 (0.37,1.41)	0.312
10-27	Malignant Systemic Neoplasms (Prostate)	0.52 (0.30,0.89)	0.007
10-28	Malignant Systemic Neoplasms (Testicles)	0.65 (0.21,1.98)	0.413
10-29	Malignant Systemic Neoplasms (Connective and Other Soft Tissues)	2.44 (0.70,8.47)	0.168
10-30	Hodgkin's Disease	--	--
10-31	Non-Hodgkin's Lymphoma	--	--
10-32	Other Malignant Systemic Neoplasms of Lymphoid and Histiocytic Tissue	--	--
10-33	All Malignant Skin and Systemic Neoplasms	0.74 (0.62.0.89)	0.001
10-34	All Skin and Systemic Neoplasms	0.84 (0.73,0.97)	0.017
10-36	PSA	0.53 (0.37,0.77)	<0.001
11-3	Inflammatory Diseases	1.03 (0.48,2.18)	0.943
11-4	Hereditary and Degenerative Disorders	1.01 (0.79,1.28)	0.952
11-5	Peripheral Disorders	1.01 (0.86,1.18)	0.915
11-6	Other Neurological Disorders	1.06 (0.90,1.24)	0.483
11-7	Smell	0.94 (0.58,1.51)	0.782
11-8	Visual Fields	3.93 (0.93,16.64)	0.040
11-9	Light Reaction	--	--

Table G-6. Summary of Unadjusted Results for Dichotomous Variables – Model 2 (Ranch Hands: Log₂ (Initial Dioxin)) (Continued)

Table Ref.	Clinical Parameter	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
11-10	Ocular Movement	0.77 (0.44,1.32)	0.315
11-11	Facial Sensation	0.45 (0.04,5.19)	0.455
11-12	Jaw Clench	0.59 (0.09,3.87)	0.539
11-13	Smile	1.38 (0.70,2.70)	0.372
11-14	Palpebral Fissure	1.15 (0.50,2.64)	0.750
11-15	Balance	1.27 (0.48,3.35)	0.638
11-16	Speech	0.29 (0.03,2.42)	0.143
11-17	Tongue Position Relative to Midline	0.59 (0.09,3.87)	0.539
11-18	Palate and Uvula Movement	0.59 (0.09,3.87)	0.539
11-19	Cranial Nerve Index	0.86 (0.63,1.17)	0.331
11-20	Neck Range of Motion	0.85 (0.72,1.02)	0.069
11-21	Pinprick	1.10 (0.86,1.41)	0.460
11-22	Light Touch	0.92 (0.66,1.28)	0.616
11-23	Muscle Status	0.87 (0.62,1.23)	0.418
11-24	Patellar Reflex	1.18 (0.82,1.71)	0.374
11-25	Achilles Reflex	1.04 (0.87,1.23)	0.688
11-26	Biceps Reflex	0.72 (0.41,1.24)	0.203
11-27	Babinski Reflex	0.89 (0.28,2.86)	0.848
11-29	Polyneuropathy Prevalence Index	1.09 (0.91,1.31)	0.344
11-30	Multiple Polyneuropathy Index	1.30 (0.98,1.73)	0.076
11-31	Confirmed Polyneuropathy Indicator	1.63 (1.05,2.53)	0.033
11-32	Tremor	1.02 (0.77,1.36)	0.869
11-33	Coordination	0.90 (0.49,1.65)	0.735
11-34	Romberg Sign	1.27 (0.48,3.35)	0.638
11-35	Gait	1.00 (0.74,1.35)	0.998
11-36	CNS Index	1.00 (0.81,1.24)	0.976
12-3	Psychoses	0.90 (0.65,1.24)	0.501
12-4	Alcohol Dependence	1.04 (0.81,1.34)	0.747
12-5	Drug Dependence	--	--
12-6	Anxiety	1.07 (0.92,1.24)	0.360
12-7	Other Neuroses	1.02 (0.89,1.18)	0.743
12-8	SCL-90-R Anxiety	0.98 (0.79,1.21)	0.847
12-9	SCL-90-R Depression	1.10 (0.91,1.32)	0.345
12-10	SCL-90-R Hostility	1.12 (0.88,1.42)	0.377
12-11	SCL-90-R Interpersonal Sensitivity	0.98 (0.81,1.18)	0.798
12-12	SCL-90-R Obsessive-Compulsive Behavior	1.02 (0.85,1.23)	0.854
12-13	SCL-90-R Paranoid Ideation	1.16 (0.91,1.47)	0.227
12-14	SCL-90-R Phobic Anxiety	1.18 (0.97,1.44)	0.100
12-15	SCL-90-R Psychoticism	1.19 (0.99,1.44)	0.065
12-16	SCL-90-R Somatization	0.98 (0.83,1.17)	0.840
12-17	SCL-90-R Global Severity Index (GSI)	1.08 (0.90,1.29)	0.415
12-18	SCL-90-R Positive Symptom Total (PST)	1.04 (0.87,1.25)	0.647
12-19	SCL-90-R Positive Symptom Distress Index (PSDI)	1.00 (0.79,1.26)	0.992
13-3	Uncharacterized Hepatitis	1.10 (0.67,1.80)	0.705
13-4	Jaundice	1.03 (0.21,5.02)	0.973
13-5	Chronic Liver Disease and Cirrhosis (Alcohol-related)	1.06 (0.78,1.45)	0.708
13-6	Chronic Liver Disease and Cirrhosis (Non-alcohol-related)	1.02 (0.61,1.70)	0.949
13-7	Liver Abscess and Sequelae of Chronic Liver Disease	1.99 (0.64,6.25)	0.277
13-8	Enlarged Liver (Hepatomegaly)	0.96 (0.56,1.65)	0.880

Table G-6. Summary of Unadjusted Results for Dichotomous Variables – Model 2 (Ranch Hands: Log₂ (Initial Dioxin)) (Continued)

Table Ref.	Clinical Parameter	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
13-9	Other Liver Disorders	1.12 (0.97,1.30)	0.119
13-10	Current Hepatomegaly	0.69 (0.36,1.31)	0.223
13-12	AST	1.08 (0.86,1.36)	0.498
13-14	ALT	1.17 (0.95,1.45)	0.140
13-16	GGT	1.00 (0.81,1.22)	0.964
13-18	Alkaline Phosphatase	0.99 (0.60,1.65)	0.971
13-20	Total Bilirubin	0.77 (0.54,1.09)	0.118
13-21	Direct Bilirubin	--	--
13-23	Lactic Dehydrogenase	0.96 (0.75,1.21)	0.709
13-25	Cholesterol	1.21 (1.01,1.45)	0.036
13-27	HDL Cholesterol	0.86 (0.66,1.12)	0.249
13-29	Cholesterol-HDL Ratio	1.25 (1.09,1.45)	0.002
13-31	Triglycerides	1.09 (0.94,1.27)	0.275
13-33	Creatine Phosphokinase	1.05 (0.83,1.32)	0.698
13-35	Serum Amylase	0.86 (0.58,1.29)	0.458
13-36	Antibodies for Hepatitis A	0.98 (0.85,1.14)	0.830
13-37	Evidence of Prior Hepatitis B	1.06 (0.86,1.31)	0.588
13-38	Current Hepatitis B	0.99 (0.17,5.76)	0.987
13-39	Antibodies for Hepatitis C	0.61 (0.24,1.60)	0.271
13-40	Stool Hemoccult	0.85 (0.59,1.24)	0.390
13-42	Prealbumin	1.44 (0.84,2.47)	0.203
13-44	Albumin	--	--
13-46	α-1-Acid Glycoprotein	1.00 (0.72,1.38)	0.991
13-50	α-2-Macroglobulin	1.22 (0.87,1.71)	0.254
13-52	Apolipoprotein B	1.14 (0.99,1.31)	0.059
13-54	C3 Complement	1.06 (0.45,2.49)	0.898
13-56	C4 Complement	--	--
13-58	Haptoglobin	1.05 (0.91,1.21)	0.506
13-60	Transferrin	0.99 (0.77,1.27)	0.931
14-3	Essential Hypertension	1.06 (0.91,1.23)	0.441
14-4	Heart Disease (Excluding Essential Hypertension)	0.79 (0.68,0.91)	0.001
14-5	Myocardial Infarction	1.01 (0.79,1.28)	0.945
14-6	Stroke or Transient Ischemia Attack	1.22 (0.68,2.16)	0.513
14-8	Systolic Blood Pressure	0.83 (0.69,0.99)	0.031
14-10	Diastolic Blood Pressure	1.04 (0.79,1.37)	0.793
14-11	Heart Sounds	1.01 (0.73,1.40)	0.958
14-12	Overall Electrocardiograph	0.90 (0.77,1.05)	0.171
14-13	Right Bundle Branch Block	0.93 (0.59,1.46)	0.747
14-14	Left Bundle Branch Block	0.21 (0.01,6.22)	0.213
14-15	Non-Specific ST- and T-Wave Changes	0.91 (0.76,1.08)	0.280
14-16	Bradycardia	0.86 (0.44,1.65)	0.631
14-17	Tachycardia	1.38 (0.72,2.68)	0.340
14-18	Arrhythmia	0.81 (0.60,1.10)	0.158
14-19	Evidence of Prior Myocardial Infarction	1.05 (0.75,1.46)	0.793
14-20	ECG: Other Diagnoses	1.53 (0.62,3.79)	0.381
14-21	Funduscopic Examination	0.93 (0.76,1.15)	0.520
14-22	Carotid Bruits	1.06 (0.70,1.59)	0.797
14-23	Radial Pulses	0.58 (0.17,1.99)	0.334
14-24	Femoral Pulses	0.97 (0.61,1.53)	0.890

Table G-6. Summary of Unadjusted Results for Dichotomous Variables – Model 2 (Ranch Hands: Log_2 (Initial Dioxin)) (Continued)

Table Ref.	Clinical Parameter	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
14-25	Popliteal Pulses	0.89 (0.57,1.38)	0.601
14-26	Dorsalis Pedis Pulses	0.90 (0.69,1.17)	0.417
14-27	Posterior Tibial Pulses	1.01 (0.77,1.33)	0.925
14-28	Leg Pulses	0.96 (0.77,1.20)	0.739
14-29	Peripheral Pulses	0.96 (0.77,1.19)	0.703
14-30	ICVI Index	0.99 (0.71,1.37)	0.948
15-14	Prothrombin Time	0.66 (0.28,1.58)	0.315
15-15	RBC Morphology	0.94 (0.73,1.21)	0.622
15-18	Absolute Neutrophils (bands) (Zero vs. Nonzero)	0.92 (0.76,1.11)	0.381
15-22	Absolute Eosinophils (Zero vs. Nonzero)	0.95 (0.77,1.17)	0.630
15-24	Absolute Basophils (Zero vs. Nonzero)	0.84 (0.73,0.97)	0.015
16-3	Past Thyroid Disease	1.13 (0.88,1.45)	0.360
16-4	Composite Diabetes Indicator	1.11 (0.94,1.32)	0.231
16-7	Thyroid Gland	0.95 (0.32,2.81)	0.923
16-8	Testicular Examination	0.93 (0.66,1.29)	0.653
16-12	Thyroxine	1.22 (0.79,1.89)	0.375
16-13	Anti-Thyroid Antibodies	0.93 (0.30,2.89)	0.905
16-15	Fasting Glucose	1.13 (0.95,1.34)	0.172
16-17	2-Hour Postprandial Glucose	0.88 (0.71,1.10)	0.267
16-18	Fasting Urinary Glucose	1.19 (0.90,1.57)	0.220
16-19	2-Hour Postprandial Urinary Glucose	0.94 (0.78,1.14)	0.535
16-23	α-1-C Hemoglobin	1.28 (1.05,1.56)	0.013
16-25	Total Testosterone	1.00 (0.80,1.26)	0.973
16-27	Free Testosterone	0.46 (0.21,0.98)	0.019
16-29	Estradiol	1.17 (1.00,1.36)	0.045
16-31	LH	0.93 (0.65,1.32)	0.668
16-33	FSH	0.94 (0.72,1.22)	0.618
17-14	ANA Test	1.08 (0.94,1.24)	0.301
17-15	ANA Thyroid Microsomal Antibody	0.77 (0.47,1.26)	0.272
17-16	MSK Smooth Muscle Antibody	0.80 (0.62,1.02)	0.061
17-17	MSK Mitochondrial Antibody	0.11 (0.01,3.47)	0.034
17-18	MSK Parietal Antibody	0.86 (0.63,1.18)	0.335
17-19	Rheumatoid Factor	0.75 (0.57,0.99)	0.033
18-3	Asthma	1.18 (0.86,1.62)	0.318
18-4	Bronchitis	1.06 (0.89,1.25)	0.513
18-5	Pneumonia	0.81 (0.63,1.05)	0.097
18-6	Thorax and Lung Abnormalities	1.06 (0.86,1.31)	0.573
18-7	X-ray Interpretation	0.89 (0.70,1.15)	0.373

[a] Adjusted for percent body fat at the time of the blood measurement for dioxin.
--: Relative risk, confidence interval, and p-value are not presented because of the sparse number of Ranch Hands with abnormalities.

Note: Relative risk for a twofold increase in initial dioxin.

Table G-7. Summary of Unadjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category)

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
9-3	Self-perception of Health	Comparison	1,213	119 (9.8)		
		Background RH	380	34 (9.0)	0.97 (0.65,1.45)	0.880
		Low RH	239	39 (16.3)	1.77 (1.19,2.62)	0.005
		High RH	243	48 (19.8)	2.14 (1.48,3.10)	<0.001
		Low plus High RH	482	87 (18.1)	1.95 (1.44,2.63)	<0.001
9-4	Appearance of Illness or Distress	Comparison	1,213	13 (1.1)		
		Background RH	381	3 (0.8)	0.74 (0.21,2.63)	0.645
		Low RH	239	7 (2.9)	2.78 (1.10,7.04)	0.031
		High RH	243	5 (2.1)	1.92 (0.67,5.45)	0.223
		Low plus High RH	482	12 (2.5)	2.30 (1.03,5.13)	0.041
9-5	Relative Age Appearance	Comparison	1,213	102 (8.4)		
		Background RH	381	39 (10.2)	1.25 (0.84,1.84)	0.271
		Low RH	239	24 (10.0)	1.22 (0.76,1.94)	0.415
		High RH	243	27 (11.1)	1.36 (0.87,2.13)	0.183
		Low plus High RH	482	51 (10.6)	1.29 (0.90,1.83)	0.166
9-7	Body Fat	Comparison	1,213	361 (29.8)		
		Background RH	381	73 (19.2)	0.56 (0.42,0.74)	<0.001
		Low RH	239	85 (35.6)	1.30 (0.97,1.74)	0.076
		High RH	243	83 (34.2)	1.22 (0.91,1.64)	0.175
		Low plus High RH	482	168 (34.9)	1.26 (1.01,1.58)	0.042
9-9	Erythrocyte Sedimentation Rate	Comparison	1,213	85 (7.0)		
		Background RH	381	25 (6.6)	1.03 (0.65,1.64)	0.908
		Low RH	239	21 (8.8)	1.25 (0.75,2.06)	0.392
		High RH	243	24 (9.9)	1.34 (0.83,2.16)	0.236
		Low plus High RH	482	45 (9.3)	1.29 (0.88,1.89)	0.190
10-3	Skin Neoplasms	Comparison	1,133	389 (34.3)		
		Background RH	359	155 (43.2)	1.49 (1.17,1.90)	0.001
		Low RH	210	94 (44.8)	1.54 (1.14,2.07)	0.005
		High RH	229	75 (32.8)	0.91 (0.67,1.23)	0.546
		Low plus High RH	439	169 (38.5)	1.17 (0.93,1.47)	0.183
10-4	Malignant Skin Neoplasms	Comparison	1,133	179 (15.8)		
		Background RH	359	65 (18.1)	1.21 (0.88,1.66)	0.237
		Low RH	210	47 (22.4)	1.52 (1.06,2.19)	0.023
		High RH	229	32 (14.0)	0.84 (0.56,1.27)	0.417
		Low plus High RH	439	79 (18.0)	1.12 (0.83,1.51)	0.457
10-5	Benign Skin Neoplasms	Comparison	1,202	258 (21.5)		
		Background RH	378	115 (30.4)	1.64 (1.26,2.13)	<0.001
		Low RH	233	58 (24.9)	1.21 (0.87,1.67)	0.261
		High RH	242	51 (21.1)	0.96 (0.68,1.34)	0.802
		Low plus High RH	475	109 (23.0)	1.07 (0.83,1.38)	0.592

Table G-7. Summary of Unadjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
10-6	Skin Neoplasms of Uncertain Behavior or Unspecified Nature	Comparison	1,133	8 (0.7)		
		Background RH	359	2 (0.6)	0.80 (0.17,3.80)	0.777
		Low RH	210	3 (1.4)	2.03 (0.53,7.72)	0.300
		High RH	229	2 (0.9)	1.22 (0.26,5.84)	0.800
		Low plus High RH	439	5 (1.1)	1.56 (0.49,4.91)	0.449
10-7	Basal Cell Carcinoma (All Sites Combined)	Comparison	1,133	150 (13.2)		
		Background RH	359	56 (15.6)	1.24 (0.89,1.73)	0.212
		Low RH	210	42 (20.0)	1.62 (1.11,2.38)	0.012
		High RH	229	23 (10.0)	0.72 (0.45,1.14)	0.160
		Low plus High RH	439	65 (14.8)	1.06 (0.76,1.47)	0.727
10-8	Basal Cell Carcinoma (Ear, Face, Head, and Neck)	Comparison	1,133	115 (10.2)		
		Background RH	359	43 (12.0)	1.21 (0.83,1.76)	0.316
		Low RH	210	33 (15.7)	1.65 (1.08,2.50)	0.020
		High RH	229	17 (7.4)	0.71 (0.41,1.20)	0.199
		Low plus High RH	439	50 (11.4)	1.06 (0.73,1.53)	0.762
10-9	Basal Cell Carcinoma (Trunk)	Comparison	1,133	46 (4.1)		
		Background RH	359	18 (5.0)	1.28 (0.73,2.25)	0.383
		Low RH	210	14 (6.7)	1.67 (0.90,3.10)	0.105
		High RH	229	8 (3.5)	0.83 (0.39,1.79)	0.638
		Low plus High RH	439	22 (5.0)	1.16 (0.68,1.99)	0.589
10-10	Basal Cell Carcinoma (Upper Extremities)	Comparison	1,133	37 (3.3)		
		Background RH	359	11 (3.1)	0.99 (0.50,1.97)	0.981
		Low RH	210	7 (3.3)	1.00 (0.44,2.27)	0.993
		High RH	229	3 (1.3)	0.37 (0.11,1.22)	0.102
		Low plus High RH	439	10 (2.3)	0.60 (0.28,1.29)	0.188
10-11	Basal Cell Carcinoma (Lower Extremities)	Comparison	1,133	5 (0.4)		
		Background RH	359	3 (0.8)	2.07 (0.48,8.80)	0.327
		Low RH	210	1 (0.5)	1.04 (0.12,8.97)	0.972
		High RH	229	1 (0.4)	0.91 (0.10,7.91)	0.932
		Low plus High RH	439	2 (0.5)	0.97 (0.19,5.06)	0.971
10-12	Squamous Cell Carcinoma	Comparison	1,133	20 (1.8)		
		Background RH	359	10 (2.8)	1.69 (0.78,3.66)	0.187
		Low RH	210	6 (2.9)	1.60 (0.63,4.04)	0.320
		High RH	229	4 (1.8)	0.94 (0.32,2.78)	0.907
		Low plus High RH	439	10 (2.3)	1.21 (0.55,2.66)	0.634
10-13	Nonmelanoma	Comparison	1,133	169 (14.9)		
		Background RH	359	62 (17.3)	1.23 (0.89,1.70)	0.203
		Low RH	210	44 (21.0)	1.49 (1.03,2.16)	0.034
		High RH	229	28 (12.2)	0.77 (0.50,1.18)	0.231
		Low plus High RH	439	72 (16.4)	1.06 (0.78,1.44)	0.729

Table G-7. Summary of Unadjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
10-14	Melanoma	Comparison	1,133	12 (1.1)		
		Background RH	359	7 (2.0)	1.76 (0.68,4.54)	0.240
		Low RH	210	5 (2.4)	2.32 (0.81,6.68)	0.117
		High RH	229	4 (1.8)	1.74 (0.55,5.49)	0.341
		Low plus High RH	439	9 (2.1)	2.00 (0.83,4.83)	0.122
10-15	Systemic Neoplasms (All Sites Combined)	Comparison	1,204	358 (29.7)		
		Background RH	376	109 (29.0)	0.98 (0.76,1.26)	0.864
		Low RH	232	83 (35.8)	1.31 (0.98,1.76)	0.072
		High RH	240	72 (30.0)	1.00 (0.74,1.36)	0.995
		Low plus High RH	472	155 (32.8)	1.14 (0.91,1.44)	0.253
10-16	Malignant Systemic Neoplasms	Comparison	1,211	73 (6.0)		
		Background RH	378	21 (5.6)	0.91 (0.55,1.51)	0.727
		Low RH	234	34 (14.5)	2.65 (1.72,4.09)	<0.001
		High RH	242	11 (4.6)	0.74 (0.39,1.43)	0.374
		Low plus High RH	476	45 (9.5)	1.39 (0.91,2.13)	0.132
10-17	Benign Systemic Neoplasms	Comparison	1,204	289 (24.0)		
		Background RH	376	93 (24.7)	1.05 (0.80,1.38)	0.710
		Low RH	232	58 (25.0)	1.05 (0.76,1.46)	0.760
		High RH	240	63 (26.3)	1.12 (0.81,1.53)	0.500
		Low plus High RH	472	121 (25.6)	1.08 (0.85,1.39)	0.521
10-18	Systemic Neoplasms of Uncertain Behavior or Unspecified Nature	Comparison	1,211	25 (2.1)		
		Background RH	378	8 (2.1)	1.08 (0.48,2.44)	0.845
		Low RH	234	6 (2.6)	1.23 (0.50,3.03)	0.657
		High RH	242	2 (0.8)	0.38 (0.09,1.61)	0.187
		Low plus High RH	476	8 (1.7)	0.67 (0.27,1.67)	0.392
10-19	Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck)	Comparison	1,211	12 (1.0)		
		Background RH	378	3 (0.8)	0.72 (0.20,2.58)	0.612
		Low RH	234	5 (2.1)	2.24 (0.78,6.43)	0.134
		High RH	242	1 (0.4)	0.46 (0.06,3.53)	0.451
		Low plus High RH	476	6 (1.3)	1.00 (0.29,3.41)	0.995
10-20	Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx)	Comparison	1,211	7 (0.6)		
		Background RH	378	1 (0.3)	0.43 (0.05,3.52)	0.431
		Low RH	234	2 (0.9)	1.51 (0.31,7.30)	0.612
		High RH	242	1 (0.4)	0.75 (0.09,6.18)	0.791
		Low plus High RH	476	3 (0.6)	1.06 (0.25,4.39)	0.938
10-21	Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum)	Comparison	1,211	0 (0.0)		
		Background RH	378	2 (0.5)	--	0.089[b]
		Low RH	234	0 (0.0)	--	--
		High RH	242	0 (0.0)	--	--
		Low plus High RH	476	0 (0.0)	--	--

Table G-7. Summary of Unadjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
10-22	Malignant Systemic Neoplasms (Thyroid Gland)	Comparison	1,211	2 (0.2)		
		Background RH	378	0 (0.0)	--	0.999[b]
		Low RH	234	2 (0.9)	5.42 (0.76,38.74)	0.092
		High RH	242	0 (0.0)	--	0.999[b]
		Low plus High RH	476	2 (0.4)	--	0.680[b]
10-23	Malignant Systemic Neoplasms (Bronchus and Lung)	Comparison	1,211	3 (0.3)		
		Background RH	378	2 (0.5)	2.14 (0.35,12.94)	0.408
		Low RH	234	8 (3.4)	14.26 (3.75,54.20)	<0.001
		High RH	242	0 (0.0)	--	0.999[b]
		Low plus High RH	476	8 (1.7)	--	0.003[b]
10-24	Malignant Systemic Neoplasms (Liver)	Comparison	1,211	2 (0.2)		
		Background RH	378	0 (0.0)	--	0.999[b]
		Low RH	234	0 (0.0)	--	0.999[b]
		High RH	242	2 (0.8)	5.70 (0.78,41.53)	0.086
		Low plus High RH	476	2 (0.4)	--	0.680[b]
10-25	Malignant Systemic Neoplasms (Colon and Rectum)	Comparison	1,211	8 (0.7)		
		Background RH	378	1 (0.3)	0.49 (0.06,3.94)	0.500
		Low RH	234	5 (2.1)	3.02 (0.97,9.45)	0.057
		High RH	242	1 (0.4)	0.51 (0.06,4.15)	0.528
		Low plus High RH	476	6 (1.3)	1.22 (0.33,4.51)	0.764
10-26	Malignant Systemic Neoplasms (Kidney and Bladder)	Comparison	1,211	6 (0.5)		
		Background RH	378	4 (1.1)	2.04 (0.57,7.34)	0.273
		Low RH	234	5 (2.1)	4.44 (1.34,14.69)	0.015
		High RH	242	2 (0.8)	1.75 (0.35,8.75)	0.497
		Low plus High RH	476	7 (1.5)	2.76 (0.87,8.80)	0.085
10-27	Malignant Systemic Neoplasms (Prostate)	Comparison	1,211	39 (3.2)		
		Background RH	378	9 (2.4)	0.73 (0.35,1.52)	0.398
		Low RH	234	12 (5.1)	1.63 (0.84,3.16)	0.150
		High RH	242	4 (1.7)	0.51 (0.18,1.44)	0.202
		Low plus High RH	476	16 (3.4)	0.90 (0.46,1.75)	0.757
10-28	Malignant Systemic Neoplasms (Testicles)	Comparison	1,211	0 (0.0)		
		Background RH	378	0 (0.0)	--	--
		Low RH	234	2 (0.9)	--	0.024[b]
		High RH	242	1 (0.4)	--	0.371[b]
		Low plus High RH	476	3 (0.6)	--	0.034[b]
10-29	Malignant Systemic Neoplasms (Connective and Other Soft Tissues)	Comparison	1,211	2 (0.2)		
		Background RH	378	0 (0.0)	--	0.999[b]
		Low RH	234	0 (0.0)	--	0.999[b]
		High RH	242	1 (0.4)	2.34 (0.21,26.43)	0.493
		Low plus High RH	476	1 (0.2)	--	0.999[b]

Table G-7. Summary of Unadjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
10-30	Hodgkin's Disease	Comparison	1,211	3 (0.3)		
		Background RH	378	1 (0.3)	0.92 (0.09,9.02)	0.945
		Low RH	234	0 (0.0)	--	0.999[b]
		High RH	242	0 (0.0)	--	0.999[b]
		Low plus High RH	476	0 (0.0)	--	0.656[b]
10-31	Non-Hodgkin's Lymphoma	Comparison	1,211	3 (0.3)		
		Background RH	378	1 (0.3)	0.92 (0.09,9.02)	0.944
		Low RH	234	0 (0.0)	--	0.999[b]
		High RH	242	0 (0.0)	--	0.999[b]
		Low plus High RH	476	0 (0.0)	--	0.656[b]
10-32	Other Malignant Systemic Neoplasms of Lymphoid and Histiocytic Tissue	Comparison	1,211	2 (0.2)		
		Background RH	378	2 (0.5)	2.64 (0.37,19.03)	0.336
		Low RH	234	0 (0.0)	--	0.999[b]
		High RH	242	0 (0.0)	--	0.999[b]
		Low plus High RH	476	0 (0.0)	--	0.919[b]
10-33	All Malignant Skin and Systemic Neoplasms	Comparison	1,200	226 (18.8)		
		Background RH	375	76 (20.3)	1.12 (0.83,1.49)	0.464
		Low RH	228	68 (29.8)	1.82 (1.33,2.51)	<0.001
		High RH	241	41 (17.0)	0.87 (0.60,1.26)	0.457
		Low plus High RH	469	109 (23.2)	1.25 (0.96,1.62)	0.103
10-34	All Skin and Systemic Neoplasms	Comparison	1,193	602 (50.5)		
		Background RH	374	211 (56.4)	1.30 (1.03,1.64)	0.030
		Low RH	227	137 (60.4)	1.49 (1.11,1.99)	0.007
		High RH	239	122 (51.1)	1.01 (0.76,1.33)	0.969
		Low plus High RH	466	259 (55.6)	1.22 (0.98,1.51)	0.076
10-36	PSA	Comparison	1,152	71 (6.2)		
		Background RH	365	20 (5.5)	0.85 (0.51,1.42)	0.526
		Low RH	222	22 (9.9)	1.69 (1.02,2.79)	0.040
		High RH	236	12 (5.1)	0.85 (0.45,1.59)	0.603
		Low plus High RH	458	34 (7.4)	1.18 (0.76,1.84)	0.454
11-3	Inflammatory Diseases	Comparison	1,204	1 (0.1)		
		Background RH	380	3 (0.8)	8.82 (0.91,85.93)	0.061
		Low RH	239	2 (0.8)	10.31 (0.93,114.27)	0.057
		High RH	240	2 (0.8)	10.86 (0.97,121.25)	0.053
		Low plus High RH	479	4 (0.8)	10.58 (1.18,95.25)	0.035
11-4	Hereditary and Degenerative Diseases	Comparison	1,211	107 (8.8)		
		Background RH	380	37 (9.7)	1.08 (0.73,1.61)	0.697
		Low RH	239	21 (8.8)	1.00 (0.61,1.63)	0.999
		High RH	240	22 (9.2)	1.07 (0.66,1.73)	0.792
		Low plus High RH	479	43 (9.0)	1.03 (0.71,1.50)	0.864

Table G-7. Summary of Unadjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
11-5	Peripheral Disorders	Comparison	1,209	233 (19.3)		
		Background RH	377	65 (17.2)	0.91 (0.67,1.23)	0.531
		Low RH	239	61 (25.5)	1.42 (1.03,1.97)	0.033
		High RH	240	59 (24.6)	1.32 (0.95,1.83)	0.097
		Low plus High RH	479	120 (25.1)	1.37 (1.07,1.76)	0.014
11-6	Other Neurological Disorders	Comparison	1,206	204 (16.9)		
		Background RH	377	59 (15.7)	0.88 (0.64,1.21)	0.442
		Low RH	239	55 (23.0)	1.48 (1.06,2.07)	0.023
		High RH	239	58 (24.3)	1.62 (1.16,2.26)	0.005
		Low plus High RH	478	113 (23.6)	1.55 (1.19,2.01)	0.001
11-7	Smell	Comparison	1,209	18 (1.5)		
		Background RH	378	8 (2.1)	1.42 (0.61,3.31)	0.420
		Low RH	238	7 (2.9)	2.01 (0.83,4.86)	0.122
		High RH	239	4 (1.7)	1.14 (0.38,3.40)	0.821
		Low plus High RH	477	11 (2.3)	1.51 (0.69,3.29)	0.300
11-8	Visual Fields	Comparison	1,207	5 (0.4)		
		Background RH	380	1 (0.3)	0.70 (0.08,6.09)	0.746
		Low RH	239	0 (0.0)	--	0.694[b]
		High RH	240	1 (0.4)	0.92 (0.11,8.03)	0.940
		Low plus High RH	479	1 (0.2)	--	0.853[b]
11-9	Light Reaction	Comparison	1,209	11 (0.9)		
		Background RH	376	1 (0.3)	0.30 (0.04,2.35)	0.252
		Low RH	239	0 (0.0)	--	0.283[b]
		High RH	239	0 (0.0)	--	0.283[b]
		Low plus High RH	478	0 (0.0)	--	0.079[b]
11-10	Ocular Movement	Comparison	1,211	14 (1.2)		
		Background RH	380	4 (1.1)	0.93 (0.30,2.85)	0.896
		Low RH	239	5 (2.1)	1.82 (0.65,5.10)	0.256
		High RH	240	5 (2.1)	1.79 (0.63,5.04)	0.271
		Low plus High RH	479	10 (2.1)	1.80 (0.79,4.10)	0.159
11-11	Facial Sensation	Comparison	1,210	2 (0.2)		
		Background RH	379	1 (0.3)	1.77 (0.16,19.96)	0.646
		Low RH	239	1 (0.4)	2.46 (0.22,27.39)	0.463
		High RH	240	0 (0.0)	--	0.999[b]
		Low plus High RH	479	1 (0.2)	--	0.999[b]
11-12	Jaw Clench	Comparison	1,211	0 (0.0)		
		Background RH	380	1 (0.3)	--	0.540[b]
		Low RH	239	1 (0.4)	--	0.366[b]
		High RH	240	0 (0.0)	--	--
		Low plus High RH	479	1 (0.2)	--	0.631[b]

Table G-7. Summary of Unadjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
11-13	Smile	Comparison	1,211	4 (0.3)		
		Background RH	380	3 (0.8)	2.61 (0.57,11.87)	0.214
		Low RH	239	2 (0.8)	2.49 (0.45,13.68)	0.295
		High RH	240	2 (0.8)	2.35 (0.42,13.05)	0.328
		Low plus High RH	479	4 (0.8)	2.42 (0.60,9.77)	0.215
11-14	Palpebral Fissure	Comparison	1,211	12 (1.0)		
		Background RH	380	4 (1.1)	1.20 (0.38,3.78)	0.759
		Low RH	239	2 (0.8)	0.81 (0.18,3.66)	0.785
		High RH	240	1 (0.4)	0.37 (0.05,2.91)	0.347
		Low plus High RH	479	3 (0.6)	0.55 (0.14,2.10)	0.381
11-15	Balance	Comparison	1,210	7 (0.6)		
		Background RH	380	5 (1.3)	2.52 (0.78,8.10)	0.121
		Low RH	239	1 (0.4)	0.70 (0.09,5.74)	0.741
		High RH	240	1 (0.4)	0.66 (0.08,5.43)	0.699
		Low plus High RH	479	2 (0.4)	0.68 (0.14,3.31)	0.633
11-16	Speech	Comparison	1,211	9 (0.7)		
		Background RH	380	2 (0.5)	0.81 (0.17,3.83)	0.793
		Low RH	239	2 (0.8)	1.07 (0.23,5.02)	0.929
		High RH	240	0 (0.0)	--	0.374[b]
		Low plus High RH	479	2 (0.4)	--	0.678[b]
11-17	Tongue Position Relative to Midline	Comparison	1,211	0 (0.0)		
		Background RH	380	1 (0.3)	--	0.540[b]
		Low RH	239	1 (0.4)	--	0.366[b]
		High RH	240	0 (0.0)	--	--
		Low plus High RH	479	1 (0.2)	--	0.631[b]
11-18	Palate and Uvula Movement	Comparison	1,211	0 (0.0)		
		Background RH	380	0 (0.0)	--	--
		Low RH	239	1 (0.4)	--	0.366[b]
		High RH	240	0 (0.0)	--	--
		Low plus High RH	479	1 (0.2)	--	0.631[b]
11-19	Cranial Nerve Index	Comparison	1,207	68 (5.6)		
		Background RH	371	25 (6.7)	1.27 (0.79,2.05)	0.329
		Low RH	236	19 (8.1)	1.45 (0.86,2.47)	0.166
		High RH	236	11 (4.7)	0.78 (0.41,1.51)	0.469
		Low plus High RH	472	30 (6.4)	1.07 (0.68,1.69)	0.776
11-20	Neck Range of Motion	Comparison	1,211	180 (14.9)		
		Background RH	380	60 (15.8)	1.16 (0.84,1.60)	0.366
		Low RH	239	56 (23.4)	1.73 (1.23,2.43)	0.002
		High RH	240	47 (19.6)	1.31 (0.91,1.87)	0.142
		Low plus High RH	479	103 (21.5)	1.50 (1.15,1.97)	0.003

Table G-7. Summary of Unadjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
11-21	Pinprick	Comparison	1,149	63 (5.5)		
		Background RH	362	19 (5.3)	1.03 (0.61,1.76)	0.900
		Low RH	226	15 (6.6)	1.20 (0.67,2.15)	0.542
		High RH	227	21 (9.3)	1.64 (0.98,2.76)	0.062
		Low plus High RH	453	36 (8.0)	1.40 (0.91,2.16)	0.123
11-22	Light Touch	Comparison	1,149	43 (3.7)		
		Background RH	362	13 (3.6)	1.01 (0.54,1.92)	0.965
		Low RH	226	12 (5.3)	1.42 (0.74,2.74)	0.295
		High RH	227	11 (4.9)	1.25 (0.63,2.46)	0.528
		Low plus High RH	453	23 (5.1)	1.33 (0.79,2.24)	0.283
11-23	Muscle Status	Comparison	1,210	35 (2.9)		
		Background RH	380	14 (3.7)	1.23 (0.65,2.31)	0.530
		Low RH	239	14 (5.9)	2.11 (1.12,3.99)	0.021
		High RH	240	10 (4.2)	1.52 (0.74,3.12)	0.254
		Low plus High RH	479	24 (5.0)	1.79 (1.05,3.06)	0.033
11-24	Patellar Reflex	Comparison	1,209	33 (2.7)		
		Background RH	380	9 (2.4)	0.91 (0.43,1.93)	0.812
		Low RH	238	7 (2.9)	1.06 (0.46,2.44)	0.882
		High RH	240	8 (3.3)	1.17 (0.53,2.58)	0.693
		Low plus High RH	478	15 (3.1)	1.12 (0.60,2.08)	0.727
11-25	Achilles Reflex	Comparison	1,206	197 (16.3)		
		Background RH	379	57 (15.0)	0.99 (0.72,1.37)	0.963
		Low RH	239	46 (19.3)	1.20 (0.84,1.71)	0.325
		High RH	240	47 (19.6)	1.16 (0.81,1.65)	0.425
		Low plus High RH	479	93 (19.4)	1.18 (0.89,1.55)	0.247
11-26	Biceps Reflex	Comparison	1,210	12 (1.0)		
		Background RH	380	2 (0.5)	0.61 (0.14,2.77)	0.524
		Low RH	239	7 (2.9)	2.88 (1.12,7.44)	0.029
		High RH	240	3 (1.3)	1.10 (0.30,3.96)	0.887
		Low plus High RH	479	10 (2.1)	1.78 (0.73,4.35)	0.209
11-27	Babinski Reflex	Comparison	1,208	11 (0.9)		
		Background RH	380	5 (1.3)	1.48 (0.50,4.33)	0.477
		Low RH	239	1 (0.4)	0.46 (0.06,3.55)	0.452
		High RH	240	1 (0.4)	0.45 (0.06,3.50)	0.444
		Low plus High RH	479	2 (0.4)	0.45 (0.10,2.05)	0.303
11-29	Polyneuropathy Prevalence Index	Comparison	1,147	175 (15.3)		
		Background RH	361	47 (13.0)	0.89 (0.63,1.27)	0.530
		Low RH	226	38 (16.8)	1.10 (0.75,1.62)	0.618
		High RH	227	42 (18.5)	1.18 (0.81,1.72)	0.376
		Low plus High RH	453	80 (17.7)	1.14 (0.85,1.53)	0.370

Table G-7. Summary of Unadjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
11-30	Multiple Polyneuropathy Index	Comparison	1,147	36 (3.1)		
		Background RH	361	14 (3.9)	1.29 (0.68,2.43)	0.432
		Low RH	226	10 (4.4)	1.42 (0.69,2.90)	0.340
		High RH	227	15 (6.6)	2.12 (1.14,3.95)	0.018
		Low plus High RH	453	25 (5.5)	1.73 (1.02,2.94)	0.042
11-31	Confirmed Polyneuropathy Indicator	Comparison	1,141	7 (0.6)		
		Background RH	358	2 (0.6)	1.06 (0.22,5.16)	0.944
		Low RH	224	3 (1.3)	2.08 (0.53,8.17)	0.293
		High RH	223	6 (2.7)	3.89 (1.28,11.86)	0.017
		Low plus High RH	447	9 (2.0)	2.85 (1.02,7.97)	0.047
11-32	Tremor	Comparison	1,211	90 (7.4)		
		Background RH	380	30 (7.9)	1.05 (0.68,1.62)	0.821
		Low RH	239	14 (5.9)	0.78 (0.43,1.39)	0.396
		High RH	240	16 (6.7)	0.90 (0.52,1.57)	0.713
		Low plus High RH	479	30 (6.3)	0.84 (0.55,1.29)	0.417
11-33	Coordination	Comparison	1,209	30 (2.5)		
		Background RH	380	12 (3.2)	1.33 (0.67,2.65)	0.412
		Low RH	239	4 (1.7)	0.66 (0.23,1.90)	0.443
		High RH	240	3 (1.3)	0.48 (0.15,1.59)	0.231
		Low plus High RH	479	7 (1.5)	0.56 (0.24,1.30)	0.181
11-34	Romberg Sign	Comparison	1,210	7 (0.6)		
		Background RH	380	5 (1.3)	2.52 (0.78,8.10)	0.121
		Low RH	239	1 (0.4)	0.70 (0.09,5.74)	0.741
		High RH	240	1 (0.4)	0.66 (0.08,5.43)	0.699
		Low plus High RH	479	2 (0.4)	0.68 (0.14,3.31)	0.633
11-35	Gait	Comparison	1,211	55 (4.5)		
		Background RH	380	23 (6.1)	1.50 (0.91,2.49)	0.115
		Low RH	239	11 (4.6)	0.98 (0.51,1.91)	0.963
		High RH	240	15 (6.3)	1.28 (0.71,2.32)	0.414
		Low plus High RH	479	26 (5.4)	1.12 (0.69,1.83)	0.640
11-36	CNS Index	Comparison	1,210	146 (12.1)		
		Background RH	380	52 (13.7)	1.18 (0.84,1.66)	0.339
		Low RH	239	24 (10.0)	0.81 (0.51,1.28)	0.363
		High RH	240	30 (12.5)	1.02 (0.67,1.56)	0.923
		Low plus High RH	479	54 (11.3)	0.91 (0.65,1.27)	0.576
12-3	Psychoses	Comparison	1,211	47 (3.9)		
		Background RH	381	10 (2.6)	0.71 (0.35,1.43)	0.339
		Low RH	239	12 (5.0)	1.29 (0.67,2.47)	0.447
		High RH	240	12 (5.0)	1.23 (0.64,2.36)	0.535
		Low plus High RH	479	24 (5.0)	1.26 (0.76,2.09)	0.373

Table G-7. Summary of Unadjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
12-4	Alcohol Dependence	Comparison	1,210	80 (6.6)		
		Background RH	381	24 (6.3)	0.93 (0.58,1.50)	0.767
		Low RH	239	18 (7.5)	1.16 (0.68,1.97)	0.594
		High RH	240	20 (8.3)	1.31 (0.78,2.18)	0.307
		Low plus High RH	479	38 (7.9)	1.23 (0.82,1.84)	0.316
12-5	Drug Dependence	Comparison	1,211	4 (0.3)		
		Background RH	381	2 (0.5)	1.32 (0.24,7.34)	0.749
		Low RH	239	0 (0.0)	--	0.830[b]
		High RH	240	0 (0.0)	--	0.828[b]
		Low plus High RH	479	0 (0.0)	--	0.481[b]
12-6	Anxiety	Comparison	1,208	328 (27.2)		
		Background RH	379	86 (22.7)	0.78 (0.60,1.03)	0.083
		Low RH	238	70 (29.4)	1.12 (0.82,1.52)	0.473
		High RH	239	73 (30.5)	1.18 (0.87,1.60)	0.279
		Low plus High RH	477	143 (30.0)	1.15 (0.91,1.45)	0.240
12-7	Other Neuroses	Comparison	1,202	637 (53.0)		
		Background RH	374	170 (45.5)	0.75 (0.60,0.95)	0.018
		Low RH	237	143 (60.3)	1.34 (1.01,1.79)	0.041
		High RH	237	149 (62.9)	1.48 (1.11,1.97)	0.008
		Low plus High RH	474	292 (61.6)	1.41 (1.13,1.75)	0.002
12-8	SCL-90-R Anxiety	Comparison	1,211	133 (11.0)		
		Background RH	381	27 (7.1)	0.65 (0.42,1.00)	0.051
		Low RH	239	26 (10.9)	0.98 (0.63,1.53)	0.919
		High RH	239	29 (12.1)	1.07 (0.70,1.65)	0.756
		Low plus High RH	478	55 (11.5)	1.02 (0.73,1.43)	0.895
12-9	SCL-90-R Depression	Comparison	1,211	194 (16.0)		
		Background RH	381	43 (11.3)	0.70 (0.49,1.00)	0.052
		Low RH	239	30 (12.6)	0.74 (0.49,1.12)	0.156
		High RH	239	41 (17.2)	1.03 (0.71,1.50)	0.862
		Low plus High RH	478	71 (14.9)	0.88 (0.65,1.18)	0.383
12-10	SCL-90-R Hostility	Comparison	1,211	107 (8.8)		
		Background RH	381	22 (5.8)	0.66 (0.41,1.07)	0.090
		Low RH	239	16 (6.7)	0.73 (0.42,1.26)	0.261
		High RH	239	23 (9.6)	1.05 (0.65,1.70)	0.828
		Low plus High RH	478	39 (8.2)	0.88 (0.60,1.30)	0.512
12-11	SCL-90-R Interpersonal Sensitivity	Comparison	1,211	198 (16.4)		
		Background RH	381	37 (9.7)	0.57 (0.39,0.83)	0.003
		Low RH	239	36 (15.1)	0.90 (0.61,1.32)	0.586
		High RH	239	43 (18.0)	1.08 (0.75,1.56)	0.672
		Low plus High RH	478	79 (16.5)	0.99 (0.74,1.31)	0.923

Table G-7. Summary of Unadjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
12-12	SCL-90-R Obsessive-Compulsive Behavior	Comparison	1,211	198 (16.4)		
		Background RH	381	43 (11.3)	0.68 (0.48,0.97)	0.032
		Low RH	239	38 (15.9)	0.96 (0.65,1.40)	0.821
		High RH	239	39 (16.3)	0.96 (0.66,1.40)	0.831
		Low plus High RH	478	77 (16.1)	0.96 (0.72,1.28)	0.773
12-13	SCL-90-R Paranoid Ideation	Comparison	1,211	85 (7.0)		
		Background RH	381	17 (4.5)	0.65 (0.38,1.10)	0.110
		Low RH	239	13 (5.4)	0.75 (0.41,1.38)	0.357
		High RH	239	26 (10.9)	1.56 (0.98,2.48)	0.062
		Low plus High RH	478	39 (8.2)	1.08 (0.72,1.64)	0.703
12-14	SCL-90-R Phobic Anxiety	Comparison	1,211	126 (10.4)		
		Background RH	381	22 (5.8)	0.53 (0.33,0.85)	0.009
		Low RH	239	25 (10.5)	1.00 (0.64,1.58)	0.986
		High RH	239	37 (15.5)	1.57 (1.05,2.33)	0.027
		Low plus High RH	478	62 (13.0)	1.25 (0.90,1.74)	0.177
12-15	SCL-90-R Psychoticism	Comparison	1,211	176 (14.5)		
		Background RH	381	33 (8.7)	0.58 (0.39,0.86)	0.006
		Low RH	239	28 (11.7)	0.77 (0.51,1.18)	0.237
		High RH	239	43 (18.0)	1.25 (0.86,1.81)	0.235
		Low plus High RH	478	71 (14.9)	0.98 (0.73,1.33)	0.914
12-16	SCL-90-R Somatization	Comparison	1,211	194 (16.0)		
		Background RH	381	44 (11.6)	0.71 (0.50,1.01)	0.056
		Low RH	239	48 (20.1)	1.31 (0.92,1.86)	0.136
		High RH	239	50 (20.9)	1.34 (0.95,1.91)	0.098
		Low plus High RH	478	98 (20.5)	1.33 (1.01,1.74)	0.042
12-17	SCL-90-R Global Severity Index (GSI)	Comparison	1,211	185 (15.3)		
		Background RH	381	35 (9.2)	0.59 (0.40,0.87)	0.007
		Low RH	239	35 (14.6)	0.94 (0.63,1.39)	0.754
		High RH	239	47 (19.7)	1.30 (0.91,1.86)	0.153
		Low plus High RH	478	82 (17.2)	1.10 (0.83,1.47)	0.500
12-18	SCL-90-R Positive Symptom Total (PST)	Comparison	1,211	204 (16.9)		
		Background RH	381	36 (9.5)	0.54 (0.37,0.78)	0.001
		Low RH	239	40 (16.7)	0.98 (0.68,1.42)	0.921
		High RH	239	45 (18.8)	1.10 (0.77,1.58)	0.604
		Low plus High RH	478	85 (17.8)	1.04 (0.79,1.37)	0.790
12-19	SCL-90-R Positive Symptom Distress Index (PSDI)	Comparison	1,211	78 (6.4)		
		Background RH	381	22 (5.8)	0.90 (0.55,1.47)	0.671
		Low RH	239	19 (8.0)	1.25 (0.74,2.11)	0.399
		High RH	239	28 (11.7)	1.91 (1.21,3.02)	0.006
		Low plus High RH	478	47 (9.8)	1.55 (1.05,2.27)	0.026

Table G-7. Summary of Unadjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
13-3	Uncharacterized Hepatitis	Comparison	1,206	21 (1.7)		
		Background RH	378	8 (2.1)	1.27 (0.56,2.92)	0.568
		Low RH	237	4 (1.7)	0.96 (0.33,2.82)	0.938
		High RH	241	5 (2.1)	1.15 (0.43,3.10)	0.779
		Low plus High RH	478	9 (1.9)	1.05 (0.48,2.32)	0.902
13-4	Jaundice	Comparison	1,182	34 (2.9)		
		Background RH	370	11 (3.0)	1.05 (0.52,2.11)	0.890
		Low RH	232	0 (0.0)	--	0.017[b]
		High RH	237	1 (0.4)	0.14 (0.02,1.04)	0.055
		Low plus High RH	469	1 (0.2)	--	0.001[b]
13-5	Chronic Liver Disease and Cirrhosis (Alcohol-related)	Comparison	1,147	54 (4.7)		
		Background RH	361	16 (4.4)	0.97 (0.55,1.73)	0.924
		Low RH	226	11 (4.9)	1.02 (0.53,1.99)	0.946
		High RH	221	12 (5.4)	1.12 (0.59,2.14)	0.725
		Low plus High RH	447	23 (5.1)	1.07 (0.65,1.77)	0.788
13-6	Chronic Liver Disease and Cirrhosis (Non-alcohol-related)	Comparison	1,212	14 (1.2)		
		Background RH	381	6 (1.6)	1.64 (0.62,4.34)	0.321
		Low RH	239	3 (1.3)	1.01 (0.29,3.58)	0.986
		High RH	243	5 (2.1)	1.52 (0.53,4.32)	0.433
		Low plus High RH	482	8 (1.7)	1.24 (0.50,3.06)	0.639
13-7	Liver Abscess and Sequelae of Chronic Liver Disease	Comparison	1,213	1 (0.1)		
		Background RH	381	0 (0.0)	--	0.999[b]
		Low RH	239	0 (0.0)	--	0.999[b]
		High RH	243	1 (0.4)	5.44 (0.33,89.44)	0.236
		Low plus High RH	482	1 (0.2)	--	0.999[b]
13-8	Enlarged Liver (Hepatomegaly)	Comparison	1,211	26 (2.1)		
		Background RH	381	6 (1.6)	0.75 (0.31,1.86)	0.540
		Low RH	239	2 (0.8)	0.38 (0.09,1.62)	0.191
		High RH	242	6 (2.5)	1.12 (0.46,2.78)	0.798
		Low plus High RH	481	8 (1.7)	0.66 (0.27,1.61)	0.357
13-9	Other Liver Disorders	Comparison	1,202	299 (24.9)		
		Background RH	378	99 (26.2)	1.15 (0.88,1.50)	0.318
		Low RH	238	64 (26.9)	1.09 (0.80,1.50)	0.578
		High RH	243	83 (34.2)	1.49 (1.10,2.00)	0.009
		Low plus High RH	481	147 (30.6)	1.28 (1.01,1.62)	0.042
13-10	Current Hepatomegaly	Comparison	1,194	7 (0.6)		
		Background RH	376	3 (0.8)	1.53 (0.39,5.99)	0.543
		Low RH	236	3 (1.3)	2.10 (0.54,8.23)	0.284
		High RH	241	4 (1.7)	2.58 (0.74,8.97)	0.136
		Low plus High RH	477	7 (1.5)	2.33 (0.80,6.76)	0.119

Table G-7. Summary of Unadjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
13-12	AST	Comparison	1,194	79 (6.6)		
		Background RH	376	17 (4.5)	0.72 (0.42,1.24)	0.241
		Low RH	236	19 (8.1)	1.21 (0.72,2.04)	0.476
		High RH	240	26 (10.8)	1.60 (1.00,2.56)	0.051
		Low plus High RH	476	45 (9.5)	1.39 (0.95,2.05)	0.094
13-14	ALT	Comparison	1,194	85 (7.1)		
		Background RH	376	17 (4.5)	0.67 (0.39,1.15)	0.145
		Low RH	236	20 (8.5)	1.18 (0.71,1.97)	0.522
		High RH	240	30 (12.5)	1.74 (1.11,2.71)	0.015
		Low plus High RH	476	50 (10.5)	1.43 (0.99,2.08)	0.058
13-16	GGT	Comparison	1,194	117 (9.8)		
		Background RH	376	25 (6.6)	0.70 (0.45,1.10)	0.122
		Low RH	236	29 (12.3)	1.27 (0.82,1.96)	0.283
		High RH	240	33 (13.8)	1.38 (0.91,2.10)	0.127
		Low plus High RH	476	62 (13.0)	1.33 (0.95,1.84)	0.094
13-18	Alkaline Phosphatase	Comparison	1,194	21 (1.8)		
		Background RH	376	12 (3.2)	1.76 (0.85,3.63)	0.127
		Low RH	236	4 (1.7)	0.97 (0.33,2.86)	0.960
		High RH	240	5 (2.1)	1.24 (0.46,3.33)	0.670
		Low plus High RH	476	9 (1.9)	1.10 (0.50,2.43)	0.815
13-20	Total Bilirubin	Comparison	1,194	74 (6.2)		
		Background RH	376	21 (5.6)	0.91 (0.55,1.51)	0.724
		Low RH	236	15 (6.4)	1.02 (0.58,1.81)	0.940
		High RH	240	9 (3.8)	0.58 (0.29,1.18)	0.131
		Low plus High RH	476	24 (5.0)	0.77 (0.47,1.25)	0.286
13-21	Direct Bilirubin	Comparison	1,194	5 (0.4)		
		Background RH	376	1 (0.3)	0.88 (0.10,7.75)	0.906
		Low RH	236	0 (0.0)	--	0.695[b]
		High RH	240	0 (0.0)	--	0.686[b]
		Low plus High RH	476	0 (0.0)	--	0.359[b]
13-23	Lactic Dehydrogenase	Comparison	1,192	123 (10.3)		
		Background RH	376	36 (9.6)	1.05 (0.71,1.57)	0.794
		Low RH	236	21 (8.9)	0.81 (0.50,1.33)	0.406
		High RH	240	22 (9.2)	0.77 (0.47,1.25)	0.291
		Low plus High RH	476	43 (9.0)	0.79 (0.55,1.15)	0.214
13-25	Cholesterol	Comparison	1,194	177 (14.8)		
		Background RH	376	48 (12.8)	0.80 (0.56,1.12)	0.195
		Low RH	236	34 (14.4)	0.98 (0.66,1.46)	0.915
		High RH	240	48 (20.0)	1.51 (1.06,2.16)	0.023
		Low plus High RH	476	82 (17.2)	1.22 (0.91,1.63)	0.183

Table G-7. Summary of Unadjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
13-27	HDL Cholesterol	Comparison	1,193	88 (7.4)		
		Background RH	376	33 (8.8)	1.35 (0.88,2.05)	0.170
		Low RH	235	19 (8.1)	1.07 (0.64,1.80)	0.798
		High RH	240	19 (7.9)	0.98 (0.58,1.65)	0.937
		Low plus High RH	475	38 (8.0)	1.02 (0.69,1.53)	0.910
13-29	Cholesterol-HDL Ratio	Comparison	1,193	492 (41.2)		
		Background RH	376	136 (36.2)	0.88 (0.69,1.13)	0.321
		Low RH	235	86 (36.6)	0.80 (0.60,1.07)	0.135
		High RH	240	130 (54.2)	1.57 (1.18,2.08)	0.002
		Low plus High RH	475	216 (45.5)	1.12 (0.90,1.40)	0.295
13-31	Triglycerides	Comparison	1,194	240 (20.1)		
		Background RH	375	53 (14.1)	0.72 (0.52,1.00)	0.051
		Low RH	236	54 (22.9)	1.15 (0.82,1.62)	0.411
		High RH	240	77 (32.1)	1.74 (1.27,2.37)	<0.001
		Low plus High RH	476	131 (27.5)	1.42 (1.10,1.82)	0.006
13-33	Creatine Phosphokinase	Comparison	1,194	111 (9.3)		
		Background RH	376	26 (6.9)	0.81 (0.51,1.26)	0.345
		Low RH	236	20 (8.5)	0.87 (0.53,1.44)	0.599
		High RH	240	25 (10.4)	1.03 (0.65,1.64)	0.905
		Low plus High RH	476	45 (9.5)	0.95 (0.66,1.37)	0.781
13-35	Serum Amylase	Comparison	1,194	38 (3.2)		
		Background RH	376	8 (2.1)	0.61 (0.28,1.32)	0.210
		Low RH	236	11 (4.7)	1.51 (0.76,3.01)	0.236
		High RH	240	6 (2.5)	0.84 (0.35,2.02)	0.697
		Low plus High RH	476	17 (3.6)	1.13 (0.62,2.06)	0.701
13-36	Antibodies for Hepatitis A	Comparison	1,212	405 (33.4)		
		Background RH	381	112 (29.4)	0.84 (0.65,1.08)	0.175
		Low RH	239	84 (35.1)	1.08 (0.80,1.44)	0.619
		High RH	243	84 (34.6)	1.04 (0.78,1.39)	0.784
		Low plus High RH	482	168 (34.9)	1.06 (0.85,1.32)	0.615
13-37	Evidence of Prior Hepatitis B	Comparison	1,211	166 (13.7)		
		Background RH	381	23 (6.0)	0.42 (0.27,0.66)	<0.001
		Low RH	238	26 (10.9)	0.76 (0.49,1.18)	0.229
		High RH	243	27 (11.1)	0.76 (0.49,1.17)	0.214
		Low plus High RH	481	53 (11.0)	0.76 (0.55,1.06)	0.105
13-38	Current Hepatitis B	Comparison	1,213	2 (0.2)		
		Background RH	381	0 (0.0)	--	0.999[b]
		Low RH	239	1 (0.4)	2.52 (0.23,27.92)	0.453
		High RH	243	0 (0.0)	--	0.999[b]
		Low plus High RH	482	1 (0.2)	--	0.999[b]

Table G-7. Summary of Unadjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
13-39	Antibodies for Hepatitis C	Comparison	1,213	17 (1.4)		
		Background RH	381	5 (1.3)	0.89 (0.32,2.44)	0.819
		Low RH	239	2 (0.8)	0.60 (0.14,2.62)	0.497
		High RH	243	2 (0.8)	0.61 (0.14,2.67)	0.512
		Low plus High RH	482	4 (0.8)	0.61 (0.20,1.81)	0.369
13-40	Stool Hemoccult	Comparison	1,162	50 (4.3)		
		Background RH	365	10 (2.7)	0.68 (0.34,1.35)	0.270
		Low RH	232	11 (4.7)	1.08 (0.55,2.12)	0.814
		High RH	232	8 (3.4)	0.74 (0.35,1.59)	0.443
		Low plus High RH	464	19 (4.1)	0.90 (0.52,1.55)	0.696
13-42	Prealbumin	Comparison	1,194	10 (0.8)		
		Background RH	376	6 (1.6)	1.94 (0.69,5.41)	0.207
		Low RH	236	1 (0.4)	0.50 (0.06,3.95)	0.513
		High RH	240	5 (2.1)	2.50 (0.84,7.42)	0.099
		Low plus High RH	476	6 (1.3)	1.13 (0.33,3.90)	0.849
13-44	Albumin	Comparison	1,194	10 (0.8)		
		Background RH	376	2 (0.5)	0.68 (0.15,3.14)	0.618
		Low RH	236	0 (0.0)	--	0.325[b]
		High RH	240	0 (0.0)	--	0.318[b]
		Low plus High RH	476	0 (0.0)	--	0.099[b]
13-46	α-1-Acid Glycoprotein	Comparison	1,194	39 (3.3)		
		Background RH	376	13 (3.5)	1.00 (0.52,1.90)	0.992
		Low RH	236	11 (4.7)	1.47 (0.74,2.91)	0.272
		High RH	240	12 (5.0)	1.65 (0.85,3.21)	0.141
		Low plus High RH	476	23 (4.8)	1.56 (0.92,2.64)	0.101
13-50	α-2-Macroglobulin	Comparison	1,194	45 (3.8)		
		Background RH	376	6 (1.6)	0.46 (0.19,1.10)	0.080
		Low RH	236	7 (3.0)	0.75 (0.33,1.69)	0.492
		High RH	240	10 (4.2)	1.00 (0.49,2.03)	0.999
		Low plus High RH	476	17 (3.6)	0.87 (0.49,1.55)	0.632
13-52	Apolipoprotein B	Comparison	1,194	636 (53.3)		
		Background RH	376	174 (46.3)	0.75 (0.60,0.95)	0.017
		Low RH	236	113 (47.9)	0.81 (0.61,1.07)	0.132
		High RH	240	132 (55.0)	1.08 (0.81,1.42)	0.606
		Low plus High RH	476	245 (51.5)	0.93 (0.75,1.16)	0.524
13-54	C3 Complement	Comparison	1,194	26 (2.2)		
		Background RH	376	12 (3.2)	1.28 (0.63,2.57)	0.495
		Low RH	236	1 (0.4)	0.20 (0.03,1.46)	0.111
		High RH	240	2 (0.8)	0.44 (0.10,1.86)	0.261
		Low plus High RH	476	3 (0.6)	0.29 (0.08,1.04)	0.057

Table G-7. Summary of Unadjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
13-56	C4 Complement	Comparison	1,194	2 (0.2)		
		Background RH	376	2 (0.5)	3.46 (0.47,25.38)	0.222
		Low RH	236	0 (0.0)	--	0.999[b]
		High RH	240	0 (0.0)	--	0.999[b]
		Low plus High RH	476	0 (0.0)	--	0.913[b]
13-58	Haptoglobin	Comparison	1,194	337 (28.2)		
		Background RH	376	115 (30.6)	1.13 (0.88,1.46)	0.338
		Low RH	236	78 (33.1)	1.25 (0.93,1.69)	0.140
		High RH	240	86 (35.8)	1.41 (1.05,1.89)	0.023
		Low plus High RH	476	164 (34.5)	1.33 (1.06,1.67)	0.015
13-60	Transferrin	Comparison	1,194	133 (11.1)		
		Background RH	376	31 (8.2)	0.72 (0.48,1.09)	0.121
		Low RH	236	23 (9.7)	0.86 (0.54,1.37)	0.526
		High RH	240	16 (6.7)	0.57 (0.33,0.97)	0.039
		Low plus High RH	476	39 (8.2)	0.70 (0.48,1.02)	0.062
14-3	Essential Hypertension	Comparison	1,183	490 (41.4)		
		Background RH	372	127 (34.1)	0.86 (0.67,1.11)	0.246
		Low RH	229	94 (41.0)	0.95 (0.71,1.29)	0.758
		High RH	242	120 (49.6)	1.22 (0.91,1.63)	0.177
		Low plus High RH	471	214 (45.4)	1.08 (0.87,1.35)	0.488
14-4	Heart Disease (Excluding Essential Hypertension)	Comparison	1,195	730 (61.1)		
		Background RH	376	259 (68.9)	1.43 (1.11,1.83)	0.005
		Low RH	233	163 (70.0)	1.48 (1.09,2.00)	0.011
		High RH	243	139 (57.2)	0.84 (0.64,1.11)	0.228
		Low plus High RH	476	302 (63.4)	1.11 (0.89,1.39)	0.359
14-5	Myocardial Infarction	Comparison	1,195	98 (8.2)		
		Background RH	376	29 (7.7)	0.98 (0.63,1.51)	0.919
		Low RH	233	19 (8.2)	0.99 (0.59,1.65)	0.958
		High RH	243	24 (9.9)	1.18 (0.73,1.89)	0.496
		Low plus High RH	476	43 (9.0)	1.08 (0.74,1.58)	0.689
14-6	Stroke or Transient Ischemia Attack	Comparison	1,195	14 (1.2)		
		Background RH	376	5 (1.3)	1.13 (0.40,3.18)	0.816
		Low RH	233	1 (0.4)	0.36 (0.05,2.78)	0.330
		High RH	243	5 (2.1)	1.78 (0.63,5.02)	0.275
		Low plus High RH	476	6 (1.3)	0.82 (0.25,2.68)	0.741
14-8	Systolic Blood Pressure	Comparison	1,195	253 (21.2)		
		Background RH	376	74 (19.7)	1.00 (0.75,1.34)	0.998
		Low RH	233	59 (25.3)	1.25 (0.90,1.73)	0.188
		High RH	243	46 (18.9)	0.80 (0.56,1.14)	0.208
		Low plus High RH	476	105 (22.1)	0.99 (0.76,1.29)	0.952

Table G-7. Summary of Unadjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
14-10	Diastolic Blood Pressure	Comparison	1,195	59 (4.9)		
		Background RH	376	15 (4.0)	0.85 (0.47,1.52)	0.576
		Low RH	233	12 (5.2)	1.04 (0.55,1.96)	0.915
		High RH	243	17 (7.0)	1.37 (0.78,2.41)	0.267
		Low plus High RH	476	29 (6.1)	1.20 (0.75,1.90)	0.447
14-11	Heart Sounds	Comparison	1,195	60 (5.0)		
		Background RH	376	9 (2.4)	0.48 (0.24,0.99)	0.047
		Low RH	233	10 (4.3)	0.84 (0.42,1.67)	0.622
		High RH	243	12 (4.9)	0.94 (0.50,1.79)	0.857
		Low plus High RH	476	22 (4.6)	0.89 (0.54,1.48)	0.656
14-12	Overall Electrocardiograph	Comparison	1,195	373 (31.2)		
		Background RH	376	118 (31.4)	1.06 (0.82,1.36)	0.659
		Low RH	233	72 (30.9)	0.98 (0.72,1.33)	0.883
		High RH	243	74 (30.5)	0.92 (0.68,1.25)	0.602
		Low plus High RH	476	146 (30.7)	0.95 (0.75,1.20)	0.659
14-13	Right Bundle Branch Block	Comparison	1,195	31 (2.6)		
		Background RH	376	9 (2.4)	0.93 (0.44,1.98)	0.852
		Low RH	233	5 (2.1)	0.82 (0.32,2.14)	0.688
		High RH	243	7 (2.9)	1.10 (0.48,2.54)	0.818
		Low plus High RH	476	12 (2.5)	0.96 (0.48,1.89)	0.895
14-14	Left Bundle Branch Block	Comparison	1,195	12 (1.0)		
		Background RH	376	4 (1.1)	1.17 (0.37,3.68)	0.792
		Low RH	233	1 (0.4)	0.42 (0.05,3.23)	0.403
		High RH	243	0 (0.0)	--	0.237[b]
		Low plus High RH	476	1 (0.2)	--	0.174[b]
14-15	Non-Specific ST- and T-Wave Changes	Comparison	1,195	218 (18.2)		
		Background RH	376	59 (15.7)	0.91 (0.66,1.25)	0.545
		Low RH	233	47 (20.2)	1.12 (0.78,1.59)	0.537
		High RH	243	50 (20.6)	1.08 (0.76,1.52)	0.677
		Low plus High RH	476	97 (20.4)	1.10 (0.84,1.44)	0.502
14-16	Bradycardia	Comparison	1,195	47 (3.9)		
		Background RH	376	16 (4.3)	0.95 (0.53,1.71)	0.867
		Low RH	233	5 (2.1)	0.55 (0.21,1.39)	0.204
		High RH	243	2 (0.8)	0.23 (0.05,0.95)	0.042
		Low plus High RH	476	7 (1.5)	0.35 (0.14,0.85)	0.020
14-17	Tachycardia	Comparison	1,195	3 (0.3)		
		Background RH	376	1 (0.3)	1.33 (0.14,13.00)	0.806
		Low RH	233	0 (0.0)	--	0.999[b]
		High RH	243	4 (1.6)	5.30 (1.15,24.53)	0.033
		Low plus High RH	476	4 (0.8)	--	0.206[b]

Table G-7. Summary of Unadjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
14-18	Arrhythmia	Comparison	1,195	65 (5.4)		
		Background RH	376	18 (4.8)	0.90 (0.53,1.54)	0.703
		Low RH	233	19 (8.2)	1.54 (0.90,2.61)	0.114
		High RH	243	13 (5.3)	0.96 (0.52,1.77)	0.886
		Low plus High RH	476	32 (6.7)	1.21 (0.77,1.88)	0.409
14-19	Evidence of Prior Myocardial Infarction	Comparison	1,195	53 (4.4)		
		Background RH	376	12 (3.2)	0.75 (0.39,1.42)	0.374
		Low RH	233	11 (4.7)	1.06 (0.54,2.06)	0.867
		High RH	243	10 (4.1)	0.88 (0.44,1.76)	0.722
		Low plus High RH	476	21 (4.4)	0.96 (0.57,1.62)	0.891
14-20	ECG: Other Diagnoses	Comparison	1,195	1 (0.1)		
		Background RH	376	1 (0.3)	2.59 (0.16,41.85)	0.503
		Low RH	233	0 (0.0)	--	0.999[b]
		High RH	243	2 (0.8)	12.49 (1.10,142.56)	0.042
		Low plus High RH	476	2 (0.4)	--	0.409[b]
14-21	Funduscopic Examination	Comparison	1,194	149 (12.5)		
		Background RH	375	43 (11.5)	0.99 (0.69,1.43)	0.963
		Low RH	233	30 (12.9)	1.02 (0.67,1.56)	0.921
		High RH	243	32 (13.2)	0.98 (0.65,1.49)	0.933
		Low plus High RH	476	62 (13.0)	1.00 (0.73,1.38)	0.993
14-22	Carotid Bruits	Comparison	1,195	31 (2.6)		
		Background RH	376	9 (2.4)	0.93 (0.44,1.98)	0.853
		Low RH	233	5 (2.1)	0.82 (0.32,2.14)	0.687
		High RH	243	8 (3.3)	1.27 (0.57,2.80)	0.561
		Low plus High RH	476	13 (2.7)	1.02 (0.53,2.00)	0.943
14-23	Radial Pulses	Comparison	1,195	4 (0.3)		
		Background RH	376	4 (1.1)	2.78 (0.69,11.27)	0.153
		Low RH	233	2 (0.9)	2.64 (0.48,14.54)	0.264
		High RH	243	1 (0.4)	1.41 (0.16,12.80)	0.759
		Low plus High RH	476	3 (0.6)	1.92 (0.40,9.18)	0.414
14-24	Femoral Pulses	Comparison	1,194	15 (1.3)		
		Background RH	376	7 (1.9)	1.39 (0.56,3.45)	0.481
		Low RH	233	6 (2.6)	2.10 (0.81,5.48)	0.128
		High RH	243	6 (2.5)	2.13 (0.81,5.56)	0.125
		Low plus High RH	476	12 (2.5)	2.11 (0.98,4.56)	0.056
14-25	Popliteal Pulses	Comparison	1,193	28 (2.3)		
		Background RH	376	9 (2.4)	0.94 (0.44,2.03)	0.879
		Low RH	233	7 (3.0)	1.31 (0.56,3.03)	0.535
		High RH	243	7 (2.9)	1.33 (0.57,3.08)	0.512
		Low plus High RH	476	14 (2.9)	1.32 (0.69,2.53)	0.410

Table G-7. Summary of Unadjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
14-26	Dorsalis Pedis Pulses	Comparison	1,193	95 (8.0)		
		Background RH	376	29 (7.7)	0.91 (0.59,1.40)	0.664
		Low RH	233	22 (9.4)	1.22 (0.75,1.98)	0.429
		High RH	243	18 (7.4)	0.98 (0.58,1.65)	0.931
		Low plus High RH	476	40 (8.4)	1.09 (0.74,1.61)	0.670
14-27	Posterior Tibial Pulses	Comparison	1,191	63 (5.3)		
		Background RH	376	22 (5.9)	1.04 (0.63,1.73)	0.865
		Low RH	233	18 (7.7)	1.52 (0.88,2.61)	0.135
		High RH	243	16 (6.6)	1.34 (0.76,2.36)	0.320
		Low plus High RH	476	34 (7.1)	1.42 (0.92,2.19)	0.113
14-28	Leg Pulses	Comparison	1,191	122 (10.2)		
		Background RH	376	39 (10.4)	0.95 (0.65,1.40)	0.812
		Low RH	233	29 (12.4)	1.26 (0.82,1.94)	0.298
		High RH	243	24 (9.9)	1.01 (0.64,1.61)	0.957
		Low plus High RH	476	53 (11.1)	1.13 (0.80,1.59)	0.498
14-29	Peripheral Pulses	Comparison	1,191	125 (10.5)		
		Background RH	376	40 (10.6)	0.95 (0.65,1.39)	0.797
		Low RH	233	30 (12.9)	1.27 (0.83,1.95)	0.266
		High RH	243	25 (10.3)	1.04 (0.66,1.63)	0.880
		Low plus High RH	476	55 (11.6)	1.15 (0.82,1.61)	0.431
14-30	ICVI Index	Comparison	1,195	43 (3.6)		
		Background RH	375	9 (2.4)	0.65 (0.31,1.35)	0.249
		Low RH	233	9 (3.9)	1.08 (0.52,2.24)	0.839
		High RH	243	14 (5.8)	1.66 (0.89,3.09)	0.112
		Low plus High RH	476	23 (4.8)	1.34 (0.79,2.27)	0.272
15-14	Prothrombin Time	Comparison	987	13 (1.3)		
		Background RH	309	6 (1.9)	1.64 (0.61,4.37)	0.327
		Low RH	182	3 (1.7)	1.17 (0.33,4.19)	0.807
		High RH	193	1 (0.5)	0.34 (0.04,2.62)	0.297
		Low plus High RH	375	4 (1.1)	0.62 (0.17,2.23)	0.461
15-15	RBC Morphology	Comparison	1,211	73 (6.0)		
		Background RH	381	24 (6.3)	1.12 (0.69,1.81)	0.639
		Low RH	239	23 (9.6)	1.63 (1.00,2.67)	0.051
		High RH	239	16 (6.7)	1.05 (0.60,1.85)	0.862
		Low plus High RH	478	39 (8.2)	1.31 (0.87,1.98)	0.196
15-18	Absolute Neutrophils (bands) (Zero vs. Nonzero)	Comparison	1,211	209 (17.3)		
		Background RH	381	65 (17.1)	0.98 (0.72,1.34)	0.908
		Low RH	239	43 (18.0)	1.05 (0.73,1.51)	0.781
		High RH	239	38 (15.9)	0.91 (0.62,1.33)	0.625
		Low plus High RH	478	81 (17.0)	0.98 (0.74,1.30)	0.881

Table G-7. Summary of Unadjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
15-22	Absolute Eosinophils (Zero vs. Nonzero)	Comparison	1,211	147 (12.1)		
		Background RH	381	44 (11.6)	0.96 (0.67,1.38)	0.833
		Low RH	239	33 (13.8)	1.15 (0.77,1.73)	0.487
		High RH	239	28 (11.7)	0.95 (0.61,1.46)	0.798
		Low plus High RH	478	61 (12.8)	1.04 (0.76,1.44)	0.789
15-24	Absolute Basophils (Zero vs. Nonzero)	Comparison	1,211	649 (53.6)		
		Background RH	381	213 (55.9)	1.09 (0.86,1.38)	0.459
		Low RH	239	147 (61.5)	1.39 (1.04,1.84)	0.025
		High RH	239	130 (54.4)	1.04 (0.78,1.37)	0.796
		Low plus High RH	478	277 (58.0)	1.20 (0.97,1.49)	0.098
16-3	Thyroid Disease	Comparison	1,208	102 (8.4)		
		Background RH	378	30 (7.9)	0.97 (0.64,1.49)	0.906
		Low RH	237	15 (6.3)	0.73 (0.41,1.27)	0.263
		High RH	241	20 (8.3)	0.94 (0.57,1.56)	0.825
		Low plus High RH	478	35 (7.3)	0.83 (0.55,1.24)	0.362
16-4	Composite Diabetes Indicator	Comparison	1,195	199 (16.7)		
		Background RH	379	37 (9.8)	0.67 (0.45,0.98)	0.041
		Low RH	235	49 (20.9)	1.27 (0.88,1.84)	0.202
		High RH	240	57 (23.8)	1.33 (0.94,1.90)	0.111
		Low plus High RH	475	106 (22.3)	1.30 (0.99,1.72)	0.064
16-7	Thyroid Gland	Comparison	1,165	16 (1.4)		
		Background RH	369	4 (1.1)	0.82 (0.27,2.47)	0.718
		Low RH	233	1 (0.4)	0.31 (0.04,2.32)	0.253
		High RH	234	1 (0.4)	0.30 (0.04,2.27)	0.242
		Low plus High RH	467	2 (0.4)	0.30 (0.07,1.32)	0.112
16-8	Testicular Examination	Comparison	1,199	47 (3.9)		
		Background RH	376	14 (3.7)	0.89 (0.49,1.65)	0.722
		Low RH	237	15 (6.3)	1.68 (0.92,3.06)	0.091
		High RH	241	9 (3.7)	1.00 (0.48,2.07)	0.994
		Low plus High RH	478	24 (5.0)	1.29 (0.77,2.16)	0.333
16-12	Thyroxine	Comparison	1,161	31 (2.7)		
		Background RH	367	13 (3.5)	1.40 (0.72,2.71)	0.325
		Low RH	233	3 (1.3)	0.47 (0.14,1.55)	0.215
		High RH	234	7 (3.0)	1.08 (0.47,2.49)	0.858
		Low plus High RH	467	10 (2.1)	0.71 (0.33,1.54)	0.390
16-13	Anti-Thyroid Antibodies	Comparison	1,161	7 (0.6)		
		Background RH	367	3 (0.8)	1.20 (0.30,4.69)	0.798
		Low RH	233	1 (0.4)	0.73 (0.09,5.96)	0.768
		High RH	234	1 (0.4)	0.80 (0.10,6.56)	0.834
		Low plus High RH	467	2 (0.4)	0.76 (0.16,3.70)	0.736

Table G-7. Summary of Unadjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
16-15	Fasting Glucose	Comparison	1,212	203 (16.7)		
		Background RH	381	48 (12.6)	0.89 (0.63,1.26)	0.517
		Low RH	238	44 (18.5)	1.07 (0.73,1.56)	0.721
		High RH	242	58 (24.0)	1.35 (0.95,1.91)	0.097
		Low plus High RH	480	102 (21.3)	1.20 (0.91,1.59)	0.200
16-17	2-Hour Postprandial Glucose	Comparison	996	155 (15.6)		
		Background RH	342	47 (13.7)	0.98 (0.68,1.40)	0.906
		Low RH	186	35 (18.8)	1.27 (0.84,1.92)	0.260
		High RH	183	31 (16.9)	1.00 (0.65,1.54)	0.999
		Low plus High RH	369	66 (17.9)	1.13 (0.82,1.56)	0.468
16-18	Fasting Urinary Glucose	Comparison	1,212	51 (4.2)		
		Background RH	381	7 (1.8)	0.53 (0.24,1.19)	0.124
		Low RH	238	9 (3.8)	0.81 (0.38,1.70)	0.571
		High RH	242	18 (7.4)	1.51 (0.85,2.69)	0.160
		Low plus High RH	480	27 (5.6)	1.11 (0.66,1.85)	0.696
16-19	2-Hour Postprandial Urinary Glucose	Comparison	994	214 (21.5)		
		Background RH	341	85 (24.9)	1.20 (0.90,1.60)	0.222
		Low RH	185	52 (28.1)	1.43 (1.00,2.03)	0.050
		High RH	183	42 (23.0)	1.10 (0.75,1.60)	0.636
		Low plus High RH	368	94 (25.5)	1.25 (0.95,1.65)	0.118
16-23	α-1-C Hemoglobin	Comparison	1,212	125 (10.3)		
		Background RH	381	25 (6.6)	0.75 (0.47,1.18)	0.210
		Low RH	238	25 (10.5)	0.95 (0.60,1.53)	0.841
		High RH	242	45 (18.6)	1.73 (1.17,2.55)	0.006
		Low plus High RH	480	70 (14.6)	1.29 (0.92,1.80)	0.138
16-25	Total Testosterone	Comparison	1,189	88 (7.4)		
		Background RH	372	23 (6.2)	1.04 (0.64,1.69)	0.878
		Low RH	234	20 (8.6)	1.08 (0.64,1.84)	0.767
		High RH	238	28 (11.8)	1.40 (0.88,2.25)	0.156
		Low plus High RH	472	48 (10.2)	1.23 (0.84,1.82)	0.285
16-27	Free Testosterone	Comparison	1,189	20 (1.7)		
		Background RH	372	5 (1.3)	0.94 (0.35,2.55)	0.906
		Low RH	234	8 (3.4)	1.95 (0.84,4.52)	0.120
		High RH	238	1 (0.4)	0.21 (0.03,1.57)	0.128
		Low plus High RH	472	9 (1.9)	0.63 (0.20,1.99)	0.431
16-29	Estradiol	Comparison	1,213	343 (28.3)		
		Background RH	381	102 (26.8)	0.96 (0.74,1.25)	0.774
		Low RH	239	59 (24.7)	0.82 (0.60,1.13)	0.234
		High RH	243	73 (30.0)	1.05 (0.78,1.43)	0.731
		Low plus High RH	482	132 (27.4)	0.93 (0.74,1.18)	0.566

Table G-7. Summary of Unadjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
16-31	LH	Comparison	1,213	67 (5.5)		
		Background RH	381	27 (7.1)	1.27 (0.79,2.02)	0.322
		Low RH	239	12 (5.0)	0.91 (0.48,1.71)	0.770
		High RH	243	9 (3.7)	0.68 (0.33,1.38)	0.280
		Low plus High RH	482	21 (4.4)	0.78 (0.47,1.30)	0.345
16-33	FSH	Comparison	1,213	93 (7.7)		
		Background RH	381	35 (9.2)	1.22 (0.81,1.84)	0.341
		Low RH	239	20 (8.4)	1.10 (0.66,1.82)	0.713
		High RH	243	16 (6.6)	0.85 (0.49,1.47)	0.557
		Low plus High RH	482	36 (7.5)	0.96 (0.64,1.44)	0.860
17-14	ANA Test	Comparison	1,164	606 (52.1)		
		Background RH	371	199 (53.6)	1.05 (0.83,1.33)	0.674
		Low RH	222	105 (47.3)	0.83 (0.62,1.11)	0.202
		High RH	231	127 (55.0)	1.14 (0.85,1.51)	0.380
		Low plus High RH	453	232 (51.2)	0.97 (0.78,1.21)	0.810
17-15	ANA Thyroid Microsomal Antibody	Comparison	1,164	34 (2.9)		
		Background RH	371	12 (3.2)	1.13 (0.58,2.22)	0.717
		Low RH	222	7 (3.2)	1.08 (0.47,2.46)	0.862
		High RH	231	5 (2.2)	0.72 (0.28,1.88)	0.506
		Low plus High RH	453	12 (2.7)	0.88 (0.45,1.73)	0.709
17-16	MSK Smooth Muscle Antibody	Comparison	1,164	141 (12.1)		
		Background RH	371	52 (14.0)	1.23 (0.87,1.74)	0.235
		Low RH	222	30 (13.5)	1.12 (0.73,1.71)	0.601
		High RH	231	19 (8.2)	0.63 (0.38,1.04)	0.071
		Low plus High RH	453	49 (10.8)	0.83 (0.59,1.19)	0.315
17-17	MSK Mitochondrial Antibody	Comparison	1,164	2 (0.2)		
		Background RH	371	2 (0.5)	3.74 (0.51,27.25)	0.193
		Low RH	222	2 (0.9)	4.91 (0.68,35.44)	0.114
		High RH	231	0 (0.0)	--	0.999[b]
		Low plus High RH	453	2 (0.4)	--	0.672[b]
17-18	MSK Parietal Antibody	Comparison	1,164	50 (4.3)		
		Background RH	371	9 (2.4)	0.61 (0.29,1.25)	0.179
		Low RH	222	16 (7.2)	1.68 (0.94,3.02)	0.082
		High RH	231	10 (4.3)	0.93 (0.46,1.87)	0.843
		Low plus High RH	453	26 (5.7)	1.24 (0.75,2.05)	0.392
17-19	Rheumatoid Factor	Comparison	1,164	130 (11.2)		
		Background RH	371	46 (12.4)	1.15 (0.80,1.65)	0.458
		Low RH	222	27 (12.2)	1.10 (0.70,1.70)	0.686
		High RH	231	15 (6.5)	0.54 (0.31,0.95)	0.032
		Low plus High RH	453	42 (9.3)	0.77 (0.52,1.12)	0.170

Table G-7. Summary of Unadjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
18-3	Asthma	Comparison	1,208	42 (3.5)		
		Background RH	377	19 (5.0)	1.47 (0.84,2.58)	0.174
		Low RH	235	10 (4.3)	1.23 (0.61,2.50)	0.559
		High RH	240	11 (4.6)	1.33 (0.67,2.64)	0.408
		Low plus High RH	475	21 (4.4)	1.28 (0.75,2.19)	0.363
18-4	Bronchitis	Comparison	1,188	230 (19.4)		
		Background RH	372	84 (22.6)	1.22 (0.92,1.62)	0.174
		Low RH	228	44 (19.3)	1.00 (0.70,1.43)	0.980
		High RH	239	54 (22.6)	1.21 (0.87,1.70)	0.262
		Low plus High RH	467	98 (21.0)	1.10 (0.84,1.44)	0.479
18-5	Pneumonia	Comparison	1,168	134 (11.5)		
		Background RH	361	38 (10.5)	0.93 (0.63,1.36)	0.708
		Low RH	222	27 (12.2)	1.06 (0.68,1.65)	0.790
		High RH	236	19 (8.1)	0.66 (0.40,1.09)	0.107
		Low plus High RH	458	46 (10.0)	0.83 (0.58,1.19)	0.315
18-6	Thorax and Lung Abnormalities	Comparison	1,213	137 (11.3)		
		Background RH	381	39 (10.2)	0.82 (0.56,1.20)	0.304
		Low RH	239	31 (13.0)	1.19 (0.79,1.82)	0.408
		High RH	243	31 (12.8)	1.24 (0.82,1.89)	0.313
		Low plus High RH	482	62 (12.9)	1.22 (0.88,1.68)	0.232
18-7	X-ray Interpretation	Comparison	1,213	116 (9.6)		
		Background RH	381	53 (13.9)	1.56 (1.10,2.21)	0.013
		Low RH	239	26 (10.9)	1.15 (0.73,1.80)	0.546
		High RH	241	17 (7.1)	0.70 (0.41,1.20)	0.196
		Low plus High RH	480	43 (9.0)	0.90 (0.62,1.31)	0.576

[a] Adjusted for percent body fat at the time of the blood measurement for dioxin.
[b] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with abnormalities.
--: Relative risk, confidence interval, and p-value are not presented because of the sparse number of participants with abnormalities.

Note: Relative risk and confidence interval relative to Comparisons.
RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background: (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table G-8. Summary of Unadjusted Results for Dichotomous Variables – Model 4 (Ranch Hands: Log_2 (1987 Dioxin + 1))

Table Ref.	Clinical Parameter	Est. Relative Risk (95% C.I.)	p-Value
9-3	Self-perception of Health	1.22 (1.08,1.39)	0.002
9-4	Appearance of Illness or Distress	1.09 (0.78,1.52)	0.631
9-5	Relative Age Appearance	0.97 (0.83,1.12)	0.654
9-7	Body Fat	1.26 (1.14,1.40)	<0.001
9-9	Erythrocyte Sedimentation Rate	1.18 (1.01,1.39)	0.040
10-3	Skin Neoplasms	0.88 (0.80,0.97)	0.012
10-4	Malignant Skin Neoplasms	0.92 (0.81,1.04)	0.187
10-5	Benign Skin Neoplasms	0.85 (0.77,0.95)	0.003
10-6	Skin Neoplasms of Uncertain Behavior or Unspecified Nature	1.16 (0.72,1.86)	0.542
10-7	Basal Cell Carcinoma (All Sites Combined)	0.87 (0.76,0.99)	0.037
10-8	Basal Cell Carcinoma (Ear, Face, Head, and Neck)	0.84 (0.72,0.98)	0.021
10-9	Basal Cell Carcinoma (Trunk)	0.96 (0.77,1.19)	0.695
10-10	Basal Cell Carcinoma (Upper Extremities)	0.77 (0.56,1.07)	0.107
10-11	Basal Cell Carcinoma (Lower Extremities)	0.85 (0.45,1.59)	0.597
10-12	Squamous Cell Carcinoma	0.95 (0.70,1.29)	0.744
10-13	Nonmelanoma	0.89 (0.78,1.01)	0.074
10-14	Melanoma	1.05 (0.76,1.46)	0.761
10-15	Systemic Neoplasms (All Sites Combined)	1.02 (0.92,1.12)	0.734
10-16	Malignant Systemic Neoplasms	0.96 (0.81,1.14)	0.641
10-17	Benign Systemic Neoplasms	1.03 (0.93,1.14)	0.582
10-18	Systemic Neoplasms of Uncertain Behavior or Unspecified Nature	0.84 (0.59,1.20)	0.329
10-19	Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck)	0.85 (0.53,1.36)	0.494
10-20	Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx)	1.23 (0.66,2.29)	0.526
10-21	Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum)	0.33 (0.12,0.92)	0.038
10-22	Malignant Systemic Neoplasms (Thyroid Gland)	0.90 (0.34,2.40)	0.832
10-23	Malignant Systemic Neoplasms (Bronchus and Lung)	0.98 (0.64,1.50)	0.915
10-24	Malignant Systemic Neoplasms (Liver)	2.10 (0.92,4.78)	0.080
10-25	Malignant Systemic Neoplasms (Colon and Rectum)	1.18 (0.74,1.91)	0.495
10-26	Malignant Systemic Neoplasms (Kidney and Bladder)	1.03 (0.69,1.53)	0.902
10-27	Malignant Systemic Neoplasms (Prostate)	0.82 (0.62,1.10)	0.182
10-28	Malignant Systemic Neoplasms (Testicles)	1.22 (0.59,2.50)	0.599
10-29	Malignant Systemic Neoplasms (Connective and Other Soft Tissues)	2.36 (0.73,7.65)	0.151
10-30	Hodgkin's Disease	0.67 (0.15,2.97)	0.583
10-31	Non-Hodgkin's Lymphoma	0.60 (0.13,2.70)	0.491
10-32	Other Malignant Systemic Neoplasms of Lymphoid and Histiocytic Tissue	0.68 (0.24,1.96)	0.466
10-33	All Malignant Skin and Systemic Neoplasms	0.94 (0.84,1.05)	0.281
10-34	All Skin and Systemic Neoplasms	0.93 (0.85,1.02)	0.149
10-36	PSA	0.91 (0.75,1.10)	0.313
11-3	Inflammatory Diseases	0.97 (0.58,1.63)	0.920
11-4	Hereditary and Degenerative Disorders	0.96 (0.82,1.12)	0.590
11-5	Peripheral Disorders	1.15 (1.04,1.29)	0.010
11-6	Other Neurological Disorders	1.13 (1.01,1.26)	0.038
11-7	Smell	0.89 (0.65,1.23)	0.481
11-8	Visual Fields	1.43 (0.62,3.31)	0.421
11-9	Light Reaction	0.77 (0.18,3.29)	0.715

Table G-8. Summary of Unadjusted Results for Dichotomous Variables – Model 4 (Ranch Hands: Log₂ (1987 Dioxin + 1)) (Continued)

Table Ref.	Clinical Parameter	Est. Relative Risk (95% C.I.)	p-Value
11-10	Ocular Movement	1.09 (0.77,1.54)	0.643
11-11	Facial Sensation	0.75 (0.27,2.11)	0.572
11-12	Jaw Clench	0.92 (0.35,2.44)	0.864
11-13	Smile	1.16 (0.72,1.88)	0.541
11-14	Palpebral Fissure	1.05 (0.64,1.73)	0.840
11-15	Balance	0.88 (0.52,1.50)	0.642
11-16	Speech	0.77 (0.37,1.59)	0.462
11-17	Tongue Position Relative to Midline	0.92 (0.35,2.44)	0.864
11-18	Palate and Uvula Movement	1.13 (0.31,4.05)	0.857
11-19	Cranial Nerve Index	0.93 (0.77,1.13)	0.462
11-20	Neck Range of Motion	1.03 (0.92,1.15)	0.632
11-21	Pinprick	1.15 (0.96,1.37)	0.137
11-22	Light Touch	1.02 (0.81,1.28)	0.865
11-23	Muscle Status	1.02 (0.82,1.27)	0.863
11-24	Patellar Reflex	1.08 (0.83,1.42)	0.568
11-25	Achilles Reflex	1.07 (0.95,1.21)	0.250
11-26	Biceps Reflex	1.16 (0.80,1.68)	0.437
11-27	Babinski Reflex	0.58 (0.32,1.03)	0.056
11-29	Polyneuropathy Prevalence Index	1.09 (0.96,1.24)	0.198
11-30	Multiple Polyneuropathy Index	1.19 (0.96,1.46)	0.110
11-31	Confirmed Polyneuropathy Indicator	1.80 (1.26,2.58)	0.002
11-32	Tremor	0.94 (0.79,1.13)	0.527
11-33	Coordination	0.81 (0.58,1.13)	0.211
11-34	Romberg Sign	0.88 (0.52,1.50)	0.642
11-35	Gait	1.00 (0.83,1.22)	0.966
11-36	CNS Index	0.97 (0.84,1.12)	0.672
12-3	Psychoses	1.11 (0.89,1.39)	0.368
12-4	Alcohol Dependence	1.07 (0.90,1.28)	0.420
12-5	Drug Dependence	0.46 (0.16,1.34)	0.155
12-6	Anxiety	1.14 (1.03,1.26)	0.011
12-7	Other Neuroses	1.20 (1.09,1.32)	<0.001
12-8	SCL-90-R Anxiety	1.15 (0.99,1.34)	0.065
12-9	SCL-90-R Depression	1.15 (1.01,1.31)	0.040
12-10	SCL-90-R Hostility	1.19 (1.01,1.41)	0.045
12-11	SCL-90-R Interpersonal Sensitivity	1.12 (0.98,1.28)	0.090
12-12	SCL-90-R Obsessive-Compulsive Behavior	1.13 (1.00,1.29)	0.058
12-13	SCL-90-R Paranoid Ideation	1.21 (1.02,1.45)	0.032
12-14	SCL-90-R Phobic Anxiety	1.28 (1.11,1.48)	0.001
12-15	SCL-90-R Psychoticism	1.24 (1.08,1.42)	0.002
12-16	SCL-90-R Somatization	1.16 (1.03,1.31)	0.013
12-17	SCL-90-R Global Severity Index (GSI)	1.24 (1.09,1.41)	0.001
12-18	SCL-90-R Positive Symptom Total (PST)	1.22 (1.07,1.38)	0.003
12-19	SCL-90-R Positive Symptom Distress Index (PSDI)	1.13 (0.97,1.33)	0.130
13-3	Uncharacterized Hepatitis	0.86 (0.61,1.21)	0.377
13-4	Jaundice	0.44 (0.28,0.69)	<0.001
13-5	Chronic Liver Disease and Cirrhosis (Alcohol-related)	1.10 (0.89,1.37)	0.368
13-6	Chronic Liver Disease and Cirrhosis (Non-alcohol-related)	1.05 (0.73,1.49)	0.803
13-7	Liver Abscess and Sequelae of Chronic Liver Disease	2.30 (0.71,7.43)	0.162
13-8	Enlarged Liver (Hepatomegaly)	0.94 (0.65,1.35)	0.731

Table G-8. Summary of Unadjusted Results for Dichotomous Variables – Model 4 (Ranch Hands: Log₂ (1987 Dioxin + 1)) (Continued)

Table Ref.	Clinical Parameter	Est. Relative Risk (95% C.I.)	p-Value
13-9	Other Liver Disorders	1.10 (1.00,1.22)	0.055
13-10	Current Hepatomegaly	1.04 (0.69,1.58)	0.853
13-12	AST	1.26 (1.06,1.48)	0.008
13-14	ALT	1.33 (1.13,1.56)	0.001
13-16	GGT	1.17 (1.01,1.35)	0.034
13-18	Alkaline Phosphatase	0.79 (0.58,1.09)	0.144
13-20	Total Bilirubin	0.89 (0.72,1.10)	0.275
13-21	Direct Bilirubin	0.78 (0.18,3.33)	0.735
13-23	Lactic Dehydrogenase	1.00 (0.85,1.17)	0.989
13-25	Cholesterol	1.15 (1.02,1.30)	0.025
13-27	HDL Cholesterol	0.92 (0.78,1.09)	0.349
13-29	Cholesterol-HDL Ratio	1.22 (1.11,1.34)	<0.001
13-31	Triglycerides	1.29 (1.16,1.44)	<0.001
13-33	Creatine Phosphokinase	1.14 (0.97,1.33)	0.123
13-35	Serum Amylase	0.93 (0.70,1.22)	0.590
13-36	Antibodies for Hepatitis A	1.08 (0.98,1.19)	0.125
13-37	Evidence of Prior Hepatitis B	1.20 (1.03,1.40)	0.023
13-38	Current Hepatitis B	1.37 (0.41,4.55)	0.617
13-39	Antibodies for Hepatitis C	0.69 (0.42,1.14)	0.139
13-40	Stool Hemoccult	1.04 (0.81,1.34)	0.760
13-42	Prealbumin	1.02 (0.69,1.49)	0.931
13-44	Albumin	0.68 (0.24,1.96)	0.465
13-46	α-1-Acid Glycoprotein	1.00 (0.80,1.25)	0.986
13-50	α-2-Macroglobulin	1.37 (1.06,1.77)	0.020
13-52	Apolipoprotein B	1.12 (1.02,1.23)	0.017
13-54	C3 Complement	0.61 (0.41,0.91)	0.011
13-56	C4 Complement	0.32 (0.12,0.90)	0.033
13-58	Haptoglobin	1.03 (0.94,1.14)	0.509
13-60	Transferrin	1.03 (0.88,1.22)	0.710
14-3	Essential Hypertension	1.22 (1.11,1.34)	<0.001
14-4	Heart Disease (Excluding Essential Hypertension)	0.87 (0.79,0.96)	0.004
14-5	Myocardial Infarction	1.03 (0.87,1.21)	0.740
14-6	Stroke or Transient Ischemia Attack	0.99 (0.66,1.48)	0.957
14-8	Systolic Blood Pressure	1.00 (0.89,1.12)	0.956
14-10	Diastolic Blood Pressure	1.14 (0.94,1.39)	0.198
14-11	Heart Sounds	1.16 (0.92,1.46)	0.220
14-12	Overall Electrocardiograph	0.96 (0.87,1.06)	0.391
14-13	Right Bundle Branch Block	1.03 (0.77,1.38)	0.845
14-14	Left Bundle Branch Block	0.69 (0.35,1.36)	0.271
14-15	Non-Specific ST- and T-Wave Changes	1.06 (0.94,1.19)	0.361
14-16	Bradycardia	0.77 (0.56,1.05)	0.084
14-17	Tachycardia	1.56 (0.92,2.63)	0.111
14-18	Arrhythmia	0.99 (0.82,1.20)	0.932
14-19	Evidence of Prior Myocardial Infarction	1.09 (0.87,1.38)	0.447
14-20	ECG: Other Diagnoses	1.27 (0.63,2.59)	0.512
14-21	Funduscopic Examination	1.00 (0.87,1.15)	0.951
14-22	Carotid Bruits	1.02 (0.77,1.36)	0.897
14-23	Radial Pulses	0.75 (0.43,1.32)	0.305
14-24	Femoral Pulses	1.01 (0.75,1.38)	0.927

Table G-8. Summary of Unadjusted Results for Dichotomous Variables – Model 4 (Ranch Hands: Log_2 (1987 Dioxin + 1)) (Continued)

Table Ref.	Clinical Parameter	Est. Relative Risk (95% C.I.)	p-Value
14-25	Popliteal Pulses	0.98 (0.74,1.30)	0.891
14-26	Dorsalis Pedis Pulses	0.99 (0.84,1.17)	0.913
14-27	Posterior Tibial Pulses	1.03 (0.86,1.24)	0.746
14-28	Leg Pulses	1.00 (0.87,1.16)	0.956
14-29	Peripheral Pulses	1.00 (0.86,1.15)	0.972
14-30	ICVI Index	1.08 (0.86,1.37)	0.503
15-14	Prothrombin Time	0.86 (0.55,1.34)	0.498
15-15	RBC Morphology	1.03 (0.87,1.23)	0.698
15-18	Absolute Neutrophils (bands) (Zero vs. Nonzero)	0.99 (0.88,1.12)	0.905
15-22	Absolute Eosinophils (Zero vs. Nonzero)	1.05 (0.91,1.20)	0.528
15-24	Absolute Basophils (Zero vs. Nonzero)	0.97 (0.88,1.06)	0.496
16-3	Past Thyroid Disease	1.01 (0.85,1.20)	0.892
16-4	Composite Diabetes Indicator	1.35 (1.20,1.52)	<0.001
16-7	Thyroid Gland	0.85 (0.47,1.51)	0.562
16-8	Testicular Examination	1.01 (0.81,1.26)	0.903
16-12	Thyroxine	0.97 (0.73,1.29)	0.825
16-13	Anti-Thyroid Antibodies	0.82 (0.43,1.55)	0.535
16-15	Fasting Glucose	1.25 (1.11,1.41)	<0.001
16-17	2-Hour Postprandial Glucose	1.06 (0.92,1.22)	0.394
16-18	Fasting Urinary Glucose	1.38 (1.12,1.71)	0.004
16-19	2-Hour Postprandial Urinary Glucose	0.97 (0.86,1.10)	0.664
16-23	α-1-C Hemoglobin	1.39 (1.21,1.60)	<0.001
16-25	Total Testosterone	1.22 (1.05,1.43)	0.013
16-27	Free Testosterone	0.94 (0.65,1.36)	0.744
16-29	Estradiol	1.04 (0.94,1.15)	0.430
16-31	LH	0.84 (0.68,1.04)	0.094
16-33	FSH	0.97 (0.82,1.15)	0.712
17-14	ANA Test	0.98 (0.90,1.08)	0.732
17-15	ANA Thyroid Microsomal Antibody	0.90 (0.68,1.20)	0.486
17-16	MSK Smooth Muscle Antibody	0.88 (0.76,1.02)	0.087
17-17	MSK Mitochondrial Antibody	0.62 (0.29,1.33)	0.206
17-18	MSK Parietal Antibody	1.14 (0.92,1.42)	0.245
17-19	Rheumatoid Factor	0.81 (0.69,0.96)	0.010
18-3	Asthma	1.06 (0.86,1.31)	0.594
18-4	Bronchitis	0.97 (0.87,1.08)	0.579
18-5	Pneumonia	0.91 (0.78,1.07)	0.236
18-6	Thorax and Lung Abnormalities	1.03 (0.90,1.19)	0.653
18-7	X-ray Interpretation	0.83 (0.71,0.97)	0.015

Note: Relative risk for a twofold increase in 1987 dioxin.

Table G-9. Summary of Unadjusted Results for Polytomous Variables – Model 1 (Ranch Hands vs. Comparisons)

Table Ref.	Clinical Parameter	Contrast	Occupational Category	Number (%) Abnormal RH	Number (%) Abnormal C	Est. Relative Risk (95% C.I.)	p-Value
11-28	Polyneuropathy Severity Index	Moderate vs. None or Mild	All	21 (2.6)	13 (1.1)	2.37 (1.18,4.76)	0.015
			Officer	7 (2.2)	6 (1.3)	1.73 (0.58,5.19)	0.330
			Enlisted Flyer	7 (4.8)	2 (1.1)	4.54 (0.93,22.20)	0.062
			Enlisted Groundcrew	7 (2.0)	5 (0.9)	2.13 (0.67,6.77)	0.199
		Severe vs. None or Mild	All	4 (0.5)	1 (0.1)	5.87 (0.65,52.61)	0.114
			Officer	3 (0.9)	0 (0.0)	--	0.130[a]
			Enlisted Flyer	0 (0.0)	0 (0.0)	--	--
			Enlisted Groundcrew	1 (0.3)	1 (0.2)	1.52 (0.09,24.45)	0.766
13-48	α-1-Antitrypsin	Low vs. Normal	All	11 (1.3)	18 (1.5)	0.88 (0.41,1.87)	0.737
			Officer	8 (2.4)	11 (2.2)	1.06 (0.42,2.65)	0.908
			Enlisted Flyer	1 (0.7)	1 (0.5)	1.23 (0.08,19.83)	0.884
			Enlisted Groundcrew	2 (0.5)	6 (1.1)	0.50 (0.10,2.51)	0.403
		High vs. Normal	All	8 (0.9)	5 (0.4)	2.30 (0.75,7.06)	0.145
			Officer	2 (0.6)	0 (0.0)	--	0.327[a]
			Enlisted Flyer	1 (0.7)	2 (1.1)	0.61 (0.07,5.25)	0.657
			Enlisted Groundcrew	5 (1.4)	3 (0.5)	2.52 (0.61,10.42)	0.202
15-4	RBC Count	Low vs. Normal	All	42 (4.9)	60 (4.8)	1.01 (0.67,1.51)	0.979
			Officer	19 (5.6)	28 (5.7)	0.97 (0.53,1.77)	0.921
			Enlisted Flyer	11 (7.3)	7 (3.7)	2.03 (0.77,5.36)	0.155
			Enlisted Groundcrew	12 (3.2)	25 (4.4)	0.72 (0.36,1.45)	0.357
		High vs. Normal	All	6 (0.7)	14 (1.1)	0.62 (0.24,1.61)	0.322
			Officer	1 (0.3)	6 (1.2)	0.24 (0.03,1.98)	0.185
			Enlisted Flyer	2 (1.3)	2 (1.1)	1.29 (0.18,9.27)	0.800
			Enlisted Groundcrew	3 (0.8)	6 (1.1)	0.75 (0.19,3.02)	0.685

Table G-9. *Summary of Unadjusted Results for Polytomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)*

Table Ref.	Clinical Parameter	Contrast	Occupational Category	Number (%) Abnormal RH	Number (%) Abnormal C	Est. Relative Risk (95% C.I.)	p-Value
15-6	WBC Count	Low vs. Normal	All	51 (5.9)	62 (5.0)	1.20 (0.82,1.75)	0.353
			Officer	22 (6.5)	29 (5.9)	1.10 (0.62,1.95)	0.747
			Enlisted Flyer	10 (6.6)	6 (3.2)	2.14 (0.76,6.05)	0.150
			Enlisted Groundcrew	19 (5.1)	27 (4.8)	1.08 (0.59,1.97)	0.809
		High vs. Normal	All	31 (3.6)	45 (3.6)	1.00 (0.63,1.60)	0.988
			Officer	7 (2.1)	12 (2.4)	0.85 (0.33,2.17)	0.727
			Enlisted Flyer	8 (5.3)	10 (5.4)	1.03 (0.40,2.68)	0.954
			Enlisted Groundcrew	16 (4.3)	23 (4.0)	1.07 (0.55,2.05)	0.850
15-8	Hemoglobin	Low vs. Normal	All	62 (7.2)	79 (6.3)	1.14 (0.81,1.61)	0.458
			Officer	25 (7.3)	29 (5.9)	1.27 (0.73,2.21)	0.400
			Enlisted Flyer	16 (10.6)	13 (7.0)	1.60 (0.74,3.44)	0.230
			Enlisted Groundcrew	21 (5.6)	37 (6.5)	0.85 (0.49,1.47)	0.557
		High vs. Normal	All	3 (0.4)	7 (0.6)	0.62 (0.16,2.41)	0.493
			Officer	2 (0.6)	2 (0.4)	1.47 (0.21,10.49)	0.700
			Enlisted Flyer	1 (0.7)	0 (0.0)	--	0.899[a]
			Enlisted Groundcrew	0 (0.0)	5 (0.9)	--	0.171[a]
15-10	Hematocrit	Low vs. Normal	All	21 (2.4)	29 (2.3)	1.04 (0.59,1.84)	0.886
			Officer	8 (2.4)	12 (2.4)	0.96 (0.39,2.37)	0.928
			Enlisted Flyer	6 (4.0)	4 (2.1)	1.91 (0.53,6.88)	0.325
			Enlisted Groundcrew	7 (1.9)	13 (2.3)	0.81 (0.32,2.05)	0.659
		High vs. Normal	All	1 (0.1)	5 (0.4)	0.29 (0.03,2.47)	0.256
			Officer	0 (0.0)	2 (0.4)	--	0.647[a]
			Enlisted Flyer	1 (0.7)	0 (0.0)	--	0.907[a]
			Enlisted Groundcrew	0 (0.0)	3 (0.5)	--	0.413[a]

Table G-9. Summary of Unadjusted Results for Polytomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Contrast	Occupational Category	Number (%) Abnormal RH	Number (%) Abnormal C	Est. Relative Risk (95% C.I.)	p-Value
15-12	Platelet Count	Low vs. Normal	All	23 (2.7)	39 (3.1)	0.85 (0.50,1.43)	0.533
			Officer	16 (4.7)	9 (1.8)	2.65 (1.16,6.06)	0.021
			Enlisted Flyer	1 (0.7)	11 (6.0)	0.11 (0.01,0.83)	0.032
			Enlisted Groundcrew	6 (1.6)	19 (3.4)	0.47 (0.19,1.20)	0.115
		High vs. Normal	All	4 (0.5)	5 (0.4)	1.15 (0.31,4.29)	0.837
			Officer	1 (0.3)	3 (0.6)	0.50 (0.05,4.79)	0.545
			Enlisted Flyer	1 (0.7)	1 (0.5)	1.16 (0.07,18.72)	0.916
			Enlisted Groundcrew	2 (0.5)	1 (0.2)	3.00 (0.27,33.23)	0.370
16-5	Diabetic Severity	No Treatment vs. Nondiabetic	All	49 (5.7)	66 (5.4)	1.07 (0.73,1.57)	0.721
			Officer	16 (4.7)	25 (5.1)	0.94 (0.49,1.80)	0.859
			Enlisted Flyer	9 (6.1)	14 (7.6)	0.78 (0.33,1.87)	0.579
			Enlisted Groundcrew	24 (6.4)	27 (4.8)	1.34 (0.76,2.36)	0.314
		Diet Only vs. Nondiabetic	All	18 (2.1)	18 (1.5)	1.44 (0.75,2.79)	0.275
			Officer	8 (2.4)	6 (1.2)	1.97 (0.67,5.72)	0.215
			Enlisted Flyer	2 (1.4)	2 (1.1)	1.22 (0.17,8.76)	0.846
			Enlisted Groundcrew	8 (2.1)	10 (1.8)	1.21 (0.47,3.09)	0.697
		Oral Hypoglycemic vs. Nondiabetic	All	38 (4.4)	77 (6.3)	0.71 (0.48,1.06)	0.097
			Officer	12 (3.6)	26 (5.3)	0.68 (0.34,1.37)	0.281
			Enlisted Flyer	9 (6.1)	12 (6.5)	0.91 (0.37,2.23)	0.840
			Enlisted Groundcrew	17 (4.5)	39 (7.0)	0.66 (0.37,1.18)	0.160
		Requiring Insulin vs. Nondiabetic	All	24 (2.8)	17 (1.4)	2.04 (1.09,3.82)	0.026
			Officer	12 (3.6)	7 (1.4)	2.53 (0.98,6.50)	0.054
			Enlisted Flyer	3 (2.0)	4 (2.2)	0.91 (0.20,4.15)	0.905
			Enlisted Groundcrew	9 (2.4)	6 (1.1)	2.26 (0.80,6.41)	0.125

Table G-9. Summary of Unadjusted Results for Polytomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Contrast	Occupational Category	Number (%) Abnormal RH	Number (%) Abnormal C	Est. Relative Risk (95% C.I.)	p-Value
16-10	TSH	Abnormal Low vs. Normal	All	10 (1.2)	9 (0.8)	1.61 (0.65,3.98)	0.301
			Officer	4 (1.2)	2 (0.4)	2.92 (0.53,16.01)	0.218
			Enlisted Flyer	3 (2.1)	2 (1.1)	1.89 (0.31,11.48)	0.488
			Enlisted Groundcrew	3 (0.8)	5 (0.9)	0.91 (0.22,3.84)	0.899
		Abnormal High vs. Normal	All	36 (4.3)	37 (3.1)	1.41 (0.88,2.25)	0.149
			Officer	14 (4.3)	17 (3.6)	1.20 (0.58,2.47)	0.620
			Enlisted Flyer	3 (2.1)	6 (3.3)	0.63 (0.15,2.57)	0.519
			Enlisted Groundcrew	19 (5.1)	14 (2.6)	2.06 (1.02,4.16)	0.044
16-21	Serum Insulin	Abnormal Low vs. Normal	All	86 (12.0)	138 (13.5)	0.85 (0.62,1.15)	0.278
			Officer	36 (12.6)	69 (16.5)	0.76 (0.48,1.20)	0.235
			Enlisted Flyer	15 (12.4)	14 (9.6)	1.11 (0.49,2.51)	0.803
			Enlisted Groundcrew	35 (11.4)	55 (12.0)	0.88 (0.55,1.42)	0.613
		Abnormal High vs. Normal	All	294 (41.2)	432 (42.2)	0.92 (0.75,1.13)	0.443
			Officer	112 (39.3)	151 (36.0)	1.08 (0.78,1.49)	0.655
			Enlisted Flyer	50 (41.3)	74 (50.7)	0.70 (0.42,1.17)	0.173
			Enlisted Groundcrew	132 (42.9)	207 (45.2)	0.89 (0.65,1.21)	0.442
18-11	Loss of Vital Capacity	Mild vs. None	All	67 (7.7)	98 (7.8)	0.98 (0.71,1.35)	0.885
			Officer	24 (7.0)	32 (6.5)	1.10 (0.63,1.90)	0.737
			Enlisted Flyer	11 (7.3)	18 (9.7)	0.72 (0.33,1.58)	0.413
			Enlisted Groundcrew	32 (8.5)	48 (8.4)	1.00 (0.62,1.59)	0.990
		Moderate or Severe vs. None	All	10 (1.2)	20 (1.6)	0.71 (0.33,1.53)	0.388
			Officer	5 (1.5)	5 (1.0)	1.46 (0.42,5.10)	0.549
			Enlisted Flyer	1 (0.7)	4 (2.2)	0.29 (0.03,2.67)	0.277
			Enlisted Groundcrew	4 (1.1)	11 (1.9)	0.54 (0.17,1.72)	0.300
18-12	Obstructive Abnormality	Mild vs. None	All	276 (31.8)	368 (29.5)	1.12 (0.93,1.36)	0.237
			Officer	124 (36.4)	147 (29.8)	1.38 (1.02,1.86)	0.034
			Enlisted Flyer	49 (32.5)	72 (38.7)	0.81 (0.50,1.28)	0.363
			Enlisted Groundcrew	103 (27.3)	149 (26.2)	1.03 (0.77,1.39)	0.845

Table G-9. Summary of Unadjusted Results for Polytomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Contrast	Occupational Category	Number (%) Abnormal RH	Number (%) Abnormal C	Est. Relative Risk (95% C.I.)	p-Value
18-12	Obstructive Abnormality (continued)	Moderate vs. None	All	51 (5.9)	75 (6.0)	1.02 (0.70,1.48)	0.928
			Officer	19 (5.6)	26 (5.3)	1.20 (0.64,2.22)	0.569
			Enlisted Flyer	14 (9.3)	12 (6.5)	1.38 (0.60,3.15)	0.444
			Enlisted Groundcrew	18 (4.8)	37 (6.5)	0.72 (0.40,1.30)	0.281
		Severe vs. None	All	14 (1.6)	16 (1.3)	1.31 (0.63,2.70)	0.467
			Officer	5 (1.5)	5 (1.0)	1.64 (0.47,5.73)	0.440
			Enlisted Flyer	6 (4.0)	5 (2.7)	1.42 (0.42,4.82)	0.574
			Enlisted Groundcrew	3 (0.8)	6 (1.1)	0.75 (0.18,3.00)	0.679

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with abnormalities.

--: Relative risk, confidence interval, and p-value not presented because of the sparse number of participants with abnormalities.

Note: RH = Ranch Hand; C = Comparison.

Table G-10. Summary of Unadjusted Results for Polytomous Variables – Model 2 (Ranch Hands: Log_2 (Initial Dioxin))

Table Ref.	Clinical Parameter	Contrast	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
11-28	Polyneuropathy Severity Index	Moderate vs. None or Mild	1.29 (0.90,1.87)	0.168
		Severe vs. None or Mild	0.68 (0.23,1.98)	0.476
13-48	α-1-Antitrypsin	Low vs. Normal	0.83 (0.37,1.90)	0.667
		High vs. Normal	1.05 (0.39,2.80)	0.925
15-4	RBC Count	Low vs. Normal	0.79 (0.53,1.15)	0.220
		High vs. Normal	0.76 (0.36,1.59)	0.464
15-6	WBC Count	Low vs. Normal	0.59 (0.39,0.89)	0.012
		High vs. Normal	0.99 (0.69,1.43)	0.964
15-8	Hemoglobin	Low vs. Normal	0.74 (0.53,1.03)	0.075
		High vs. Normal	1.16 (0.24,5.60)	0.856
15-10	Hematocrit	Low vs. Normal	0.95 (0.58,1.57)	0.840
		High vs. Normal	1.17 (0.24,5.66)	0.841
15-12	Platelet Count	Low vs. Normal	0.63 (0.33,1.19)	0.152
		High vs. Normal	1.28 (0.49,3.36)	0.616
16-5	Diabetic Severity	No Treatment vs. Nondiabetic	1.14 (0.87,1.49)	0.332
		Diet Only vs. Nondiabetic	1.12 (0.74,1.71)	0.584
		Oral Hypoglycemic vs. Nondiabetic	1.13 (0.87,1.48)	0.358
		Requiring Insulin vs. Nondiabetic	1.23 (0.86,1.76)	0.250
16-10	TSH	Low vs. Normal	1.40 (0.73,2.71)	0.311
		High vs. Normal	1.27 (0.89,1.79)	0.183
16-21	Serum Insulin	Low vs. Normal	0.96 (0.70,1.32)	0.815
		High vs. Normal	1.07 (0.90,1.28)	0.447
18-11	Loss of Vital Capacity	Mild vs. None	0.88 (0.67,1.15)	0.345
		Moderate or Severe vs. None	0.73 (0.31,1.76)	0.489
18-12	Obstructive Abnormality	Mild vs. None	0.79 (0.67,0.93)	0.005
		Moderate vs. None	0.87 (0.63,1.20)	0.393
		Severe vs. None	0.53 (0.24,1.21)	0.131

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: Relative risk for a twofold increase in initial dioxin.

Table G-11. Summary of Unadjusted Results for Polytomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category)

Table Ref.	Clinical Parameter	Contrast	Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
11-28	Polyneuropathy Severity Index	Moderate vs. None or Mild	Comparison	1,146	13 (1.1)		
			Background RH	361	5 (1.4)	1.30 (0.46,3.71)	0.619
			Low RH	226	7 (3.1)	2.76 (1.09,7.02)	0.032
			High RH	227	7 (3.1)	2.64 (1.03,6.73)	0.042
			Low plus High RH	453	14 (3.1)	2.70 (1.26,5.81)	0.011
		Severe vs. None or Mild	Comparison	1,146	1 (0.1)		
			Background RH	361	1 (0.3)	3.03 (0.19,49.25)	0.435
			Low RH	226	2 (0.9)	10.54 (0.95,116.83)	0.055
			High RH	227	1 (0.4)	5.41 (0.33,87.73)	0.235
			Low plus High RH	453	3 (0.7)	7.54 (0.75,75.71)	0.086
13-48	α-1-Antitrypsin	Low vs. Normal	Comparison	1,194	17 (1.4)		
			Background RH	376	7 (1.9)	1.14 (0.47,2.79)	0.772
			Low RH	236	2 (0.8)	0.61 (0.14,2.67)	0.513
			High RH	240	2 (0.8)	0.68 (0.16,2.98)	0.610
			Low plus High RH	476	4 (0.8)	0.65 (0.22,1.93)	0.434
		High vs. Normal	Comparison	1,194	5 (0.4)		
			Background RH	376	5 (1.3)	2.48 (0.70,8.77)	0.158
			Low RH	236	1 (0.4)	1.03 (0.11,9.33)	0.976
			High RH	240	2 (0.8)	3.49 (0.64,19.06)	0.149
			Low plus High RH	476	3 (0.6)	1.91 (0.42,8.72)	0.404
15-4	RBC Count	Low vs. Normal	Comparison	1,211	55 (4.5)		
			Background RH	381	19 (5.0)	1.09 (0.64,1.87)	0.757
			Low RH	239	12 (5.0)	1.11 (0.58,2.10)	0.753
			High RH	239	9 (3.8)	0.83 (0.40,1.70)	0.603
			Low plus High RH	478	21 (4.4)	0.96 (0.57,1.61)	0.868

Table G-11. Summary of Unadjusted Results for Polytomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Contrast	Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
15-4	RBC Count (continued)	High vs. Normal	Comparison	1,211	14 (1.2)		
			Background RH	381	1 (0.3)	0.26 (0.03,1.99)	0.195
			Low RH	239	2 (0.8)	0.69 (0.15,3.06)	0.623
			High RH	239	3 (1.3)	0.94 (0.26,3.33)	0.921
			Low plus High RH	478	5 (1.1)	0.80 (0.28,2.30)	0.683
15-6	WBC Count	Low vs. Normal	Comparison	1,211	59 (4.9)		
			Background RH	381	25 (6.6)	1.22 (0.75,1.99)	0.426
			Low RH	239	20 (8.4)	1.82 (1.07,3.10)	0.027
			High RH	239	6 (2.5)	0.56 (0.24,1.32)	0.188
			Low plus High RH	478	26 (5.4)	1.01 (0.59,1.73)	0.963
		High vs. Normal	Comparison	1,211	43 (3.6)		
			Background RH	381	12 (3.2)	0.86 (0.45,1.67)	0.664
			Low RH	239	7 (2.9)	0.86 (0.38,1.94)	0.716
			High RH	239	11 (4.6)	1.32 (0.67,2.61)	0.420
			Low plus High RH	478	18 (3.8)	1.07 (0.60,1.89)	0.825
15-8	Hemoglobin	Low vs. Normal	Comparison	1,211	74 (6.1)		
			Background RH	381	30 (7.9)	1.35 (0.86,2.10)	0.188
			Low RH	239	16 (6.7)	1.09 (0.62,1.90)	0.767
			High RH	239	13 (5.4)	0.86 (0.47,1.58)	0.630
			Low plus High RH	478	29 (6.1)	0.97 (0.62,1.51)	0.887
		High vs. Normal	Comparison	1,211	7 (0.6)		
			Background RH	381	2 (0.5)	1.04 (0.21,5.12)	0.958
			Low RH	239	0 (0.0)	--	0.507[b]
			High RH	239	1 (0.4)	0.64 (0.08,5.28)	0.677
			Low plus High RH	478	1 (0.2)	--	0.547[b]

Table G-11. Summary of Unadjusted Results for Polytomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Contrast	Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
15-10	Hematocrit	Low vs. Normal	Comparison	1,211	27 (2.2)		
			Background RH	381	8 (2.1)	0.97 (0.43,2.16)	0.933
			Low RH	239	5 (2.1)	0.93 (0.35,2.43)	0.875
			High RH	239	5 (2.1)	0.91 (0.35,2.40)	0.850
			Low plus High RH	478	10 (2.1)	0.92 (0.44,1.92)	0.820
		High vs. Normal	Comparison	1,211	5 (0.4)		
			Background RH	381	0 (0.0)	--	0.464[b]
			Low RH	239	0 (0.0)	--	0.695[b]
			High RH	239	1 (0.4)	0.91 (0.10,7.96)	0.931
			Low plus High RH	478	1 (0.2)	--	0.856[b]
15-12	Platelet Count	Low vs. Normal	Comparison	1,205	35 (2.9)		
			Background RH	379	14 (3.7)	1.40 (0.74,2.66)	0.299
			Low RH	238	6 (2.5)	0.84 (0.35,2.03)	0.702
			High RH	238	2 (0.8)	0.26 (0.06,1.10)	0.067
			Low plus High RH	476	8 (1.7)	0.47 (0.20,1.13)	0.090
		High vs. Normal	Comparison	1,205	5 (0.4)		
			Background RH	379	2 (0.5)	1.02 (0.19,5.30)	0.984
			Low RH	238	0 (0.0)	--	0.693[b]
			High RH	238	2 (0.8)	2.61 (0.49,13.84)	0.261
			Low plus High RH	476	2 (0.4)	--	0.999[b]

Table G-11. Summary of Unadjusted Results for Polytomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Contrast	Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
16-5	Diabetic Severity	No Treatment vs. Nondiabetic	Comparison	1,195	63 (5.3)		
			Background RH	379	16 (4.2)	0.91 (0.51,1.61)	0.749
			Low RH	235	13 (5.5)	1.04 (0.55,1.94)	0.912
			High RH	240	19 (7.9)	1.43 (0.83,2.47)	0.202
			Low plus High RH	475	32 (6.7)	1.22 (0.77,1.92)	0.394
		Diet Only vs. Nondiabetic	Comparison	1,195	17 (1.4)		
			Background RH	379	6 (1.6)	1.23 (0.48,3.17)	0.668
			Low RH	235	5 (2.1)	1.49 (0.54,4.11)	0.437
			High RH	240	7 (2.9)	2.00 (0.81,4.92)	0.131
			Low plus High RH	475	12 (2.5)	1.73 (0.81,3.70)	0.156
		Oral Hypoglycemic vs. Nondiabetic	Comparison	1,195	72 (6.0)		
			Background RH	379	5 (1.3)	0.27 (0.11,0.69)	0.006
			Low RH	235	14 (6.0)	0.92 (0.49,1.72)	0.795
			High RH	240	18 (7.5)	1.08 (0.61,1.91)	0.799
			Low plus High RH	475	32 (6.7)	1.00 (0.63,1.58)	0.988
		Requiring Insulin vs. Nondiabetic	Comparison	1,195	17(1.4)		
			Background RH	379	8 (2.1)	1.55 (0.66,3.63)	0.318
			Low RH	235	8 (3.4)	2.43 (1.03,5.72)	0.042
			High RH	240	8 (3.3)	2.40 (1.02,5.65)	0.046
			Low plus High RH	475	16 (3.4)	2.41 (1.20,4.83)	0.013

Table G-11. Summary of Unadjusted Results for Polytomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Contrast	Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
16-10	TSH	Low vs. Normal	Comparison	1,161	9 (0.8)		
			Background RH	367	6 (1.6)	2.27 (0.80,6.50)	0.125
			Low RH	233	1 (0.4)	0.54 (0.07,4.31)	0.564
			High RH	234	3 (1.3)	1.60 (0.43,6.02)	0.485
			Low plus High RH	467	4 (0.9)	0.93 (0.25,3.48)	0.919
		High vs. Normal	Comparison	1,161	36 (3.1)		
			Background RH	367	17 (4.6)	1.46 (0.80,2.64)	0.214
			Low RH	233	7 (3.0)	0.97 (0.43,2.22)	0.951
			High RH	234	10 (4.3)	1.47 (0.72,3.02)	0.294
			Low plus High RH	467	17 (3.6)	1.20 (0.66,2.17)	0.553
16-21	Serum Insulin	Low vs. Normal	Comparison	996	131 (13.2)		
			Background RH	342	51 (14.9)	0.96 (0.66,1.39)	0.820
			Low RH	186	20 (10.8)	0.84 (0.50,1.43)	0.527
			High RH	183	13 (7.1)	0.58 (0.31,1.07)	0.082
			Low plus High RH	369	33 (8.9)	0.70 (0.45,1.07)	0.102
		High vs. Normal	Comparison	996	418 (42.0)		
			Background RH	342	122 (35.7)	0.91 (0.69,1.20)	0.507
			Low RH	186	85 (45.7)	1.14 (0.81,1.61)	0.460
			High RH	183	87 (47.5)	0.99 (0.70,1.40)	0.968
			Low plus High RH	369	172 (46.6)	1.06 (0.82,1.39)	0.643

Table G-11. Summary of Unadjusted Results for Polytomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Contrast	Dioxin Category	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)[a]	p-Value[a]
18-11	Loss of Vital Capacity	Mild vs. None	Comparison	1,211	97 (8.0)		
			Background RH	381	31 (8.1)	1.18 (0.77,1.81)	0.456
			Low RH	238	18 (7.6)	0.89 (0.52,1.51)	0.663
			High RH	243	17 (7.0)	0.75 (0.43,1.29)	0.295
			Low plus High RH	481	35 (7.3)	0.81 (0.54,1.23)	0.325
		Moderate or Severe vs. None	Comparison	1,211	18 (1.5)		
			Background RH	381	6 (1.6)	1.27 (0.50,3.27)	0.616
			Low RH	238	2 (0.8)	0.52 (0.12,2.28)	0.387
			High RH	243	2 (0.8)	0.46 (0.10,2.00)	0.297
			Low plus High RH	481	4 (0.8)	0.49 (0.16,1.46)	0.199
18-12	Obstructive Abnormality	Mild vs. None	Comparison	1,211	356 (29.4)		
			Background RH	381	131 (34.4)	1.26 (0.98,1.62)	0.071
			Low RH	238	85 (35.7)	1.38 (1.02,1.86)	0.037
			High RH	243	55 (22.6)	0.70 (0.50,0.97)	0.031
			Low plus High RH	481	140 (29.1)	0.98 (0.77,1.24)	0.838
		Moderate vs. None	Comparison	1,211	73 (6.0)		
			Background RH	381	25 (6.6)	1.14 (0.70,1.85)	0.595
			Low RH	238	13 (5.5)	1.03 (0.56,1.92)	0.915
			High RH	243	13 (5.3)	0.82 (0.44,1.52)	0.533
			Low plus High RH	481	26 (5.4)	0.92 (0.58,1.47)	0.731
		Severe vs. None	Comparison	1,211	15 (1.2)		
			Background RH	381	7 (1.8)	1.42 (0.57,3.55)	0.453
			Low RH	238	6 (2.5)	2.37 (0.90,6.24)	0.080
			High RH	243	1 (0.4)	0.33 (0.04,2.56)	0.291
			Low plus High RH	481	7 (1.5)	0.88 (0.27,2.90)	0.835

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with abnormalities.
--: Relative risk, confidence interval, and p-value are not presented because of the sparse number of participants with abnormalities.

Table G-11. Summary of Unadjusted Results for Polytomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Note: Relative risk and confidence interval relative to Comparisons.
RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background: (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table G-12. Summary of Unadjusted Results for Polytomous Variables – Model 4 (Ranch Hands: Log_2 (1987 Dioxin + 1))

Table Ref.	Clinical Parameter	Contrast	Est. Relative Risk (95% C.I.)	p-Value
11-28	Polyneuropathy Severity Index	Moderate vs. None or Mild	1.38 (1.04,1.84)	0.024
		Severe vs. None or Mild	1.13 (0.59,2.15)	0.717
13-48	α-1-Antitrypsin	Low vs. Normal	0.76 (0.49,1.19)	0.229
		High vs. Normal	0.80 (0.48,1.33)	0.393
15-4	RBC Count	Low vs. Normal	0.91 (0.73,1.14)	0.405
		High vs. Normal	1.16 (0.69,1.95)	0.566
15-6	WBC Count	Low vs. Normal	0.78 (0.63,0.96)	0.020
		High vs. Normal	0.99 (0.77,1.27)	0.957
15-8	Hemoglobin	Low vs. Normal	0.82 (0.68,1.00)	0.049
		High vs. Normal	0.47 (0.20,1.14)	0.096
15-10	Hematocrit	Low vs. Normal	0.91 (0.65,1.26)	0.568
		High vs. Normal	1.41 (0.43,4.63)	0.573
15-12	Platelet Count	Low vs. Normal	0.70 (0.50,0.96)	0.028
		High vs. Normal	0.95 (0.48,1.88)	0.879
16-5	Diabetic Severity	No Treatment vs. Nondiabetic	1.28 (1.06,1.55)	0.010
		Diet Only vs. Nondiabetic	1.27 (0.94,1.72)	0.120
		Oral Hypoglycemic vs. Nondiabetic	1.58 (1.28,1.94)	<0.001
		Requiring Insulin vs. Nondiabetic	1.15 (0.87,1.50)	0.323
16-10	TSH	Low vs. Normal	0.97 (0.63,1.48)	0.881
		High vs. Normal	0.98 (0.78,1.24)	0.894
16-21	Serum Insulin	Low vs. Normal	0.83 (0.69,1.00)	0.050
		High vs. Normal	1.16 (1.04,1.30)	0.008
18-11	Loss of Vital Capacity	Mild vs. None	0.94 (0.79,1.12)	0.480
		Moderate or Severe vs. None	0.83 (0.53,1.31)	0.430
18-12	Obstructive Abnormality	Mild vs. None	0.83 (0.75,0.92)	<0.001
		Moderate vs. None	0.86 (0.70,1.05)	0.145
		Severe vs. None	0.70 (0.47,1.04)	0.078

Note: Relative risk for a twofold increase in 1987 dioxin.

Table G-13. Summary of Adjusted Results for Continuous Variables – Model 1 (Ranch Hands vs. Comparisons)

Table Ref.	Clinical Parameter (Units)	Occupational Category	Adj. Mean RH	Adj. Mean C	Difference of Adj. Means (95% C.I.)	p-Value
9-6	Body Fat (percent)[a]	All	22.13	22.29	–0.17 --	0.481
		Officer	21.96	21.81	0.16 --	0.674
		Enlisted Flyer	21.84	22.43	–0.59 --	0.319
		Enlisted Groundcrew	22.45	22.76	–0.31 --	0.394
9-8	Erythrocyte Sedimentation Rate (mm/hr)[b]	All	5.12	5.08	0.04 --	0.850
		Officer	4.30	4.38	–0.08 --	0.789
		Enlisted Flyer	5.13	5.74	–0.60 --	0.286
		Enlisted Groundcrew	5.81	5.39	0.42 --	0.236
10-35	PSA (ng/ml)[a]	All	1.202	1.199	0.003 --	0.946
		Officer	1.157	1.194	–0.037 --	0.590
		Enlisted Flyer	1.289	1.249	0.040 --	0.719
		Enlisted Groundcrew	1.177	1.149	0.028 --	0.668
13-11	AST (U/l)[a]	All	23.36	23.17	0.18 --	0.597
		Officer	23.88	23.80	0.08 --	0.885
		Enlisted Flyer	22.79	22.87	–0.09 --	0.916
		Enlisted Groundcrew	23.32	22.95	0.37 --	0.470
13-13	ALT (U/l)[a]	All	42.29	42.09	0.20 --	0.707
		Officer	42.75	42.14	0.61 --	0.460
		Enlisted Flyer	41.72	42.84	–1.12 --	0.386
		Enlisted Groundcrew	41.96	41.66	0.30 --	0.698
13-15	GGT (U/l)[a]	All	46.80	45.47	1.33 --	0.223
		Officer	45.24	43.62	1.62 --	0.331
		Enlisted Flyer	48.28	47.66	0.62 --	0.826
		Enlisted Groundcrew	46.67	45.39	1.28 --	0.439
13-17	Alkaline Phosphatase (U/l)[a]	All	82.77	80.46	2.32 --	0.016
		Officer	78.68	76.88	1.80 --	0.215
		Enlisted Flyer	84.06	83.47	0.58 --	0.811
		Enlisted Groundcrew	85.11	81.68	3.43 --	0.021
13-19	Total Bilirubin (mg/dl)[a]	All	0.511	0.511	–0.000 --	0.963
		Officer	0.528	0.528	0.000 --	0.993
		Enlisted Flyer	0.487	0.505	–0.018 --	0.482
		Enlisted Groundcrew	0.512	0.507	0.006 --	0.727
13-22	Lactic Dehydrogenase (U/l)[a]	All	155.3	155.0	0.3 --	0.790
		Officer	154.8	155.3	–0.6 --	0.768
		Enlisted Flyer	153.1	153.9	–0.8 --	0.787
		Enlisted Groundcrew	157.8	156.3	1.5 --	0.397
13-24	Cholesterol (mg/dl)[c]	All	212.3	212.6	–0.3 --	0.850
		Officer	206.6	210.4	–3.8 --	0.141
		Enlisted Flyer	215.3	216.4	–1.2 --	0.781
		Enlisted Groundcrew	214.6	211.4	3.2 --	0.197

Table G-13. Summary of Adjusted Results for Continuous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter (Units)	Occupational Category	Adj. Mean RH	Adj. Mean C	Difference of Adj. Means (95% C.I.)	p-Value
13-26	HDL Cholesterol (mg/dl) [a]	All	47.08	46.81	0.28 --	0.600
		Officer	48.76	48.86	–0.10 --	0.907
		Enlisted Flyer	47.56	45.28	2.29 --	0.078
		Enlisted Groundcrew	45.68	45.81	–0.13 --	0.866
13-28	Cholesterol-HDL Ratio [a]	All	4.48	4.51	–0.03 --	0.546
		Officer	4.21	4.27	–0.06 --	0.446
		Enlisted Flyer	4.49	4.76	–0.27 --	0.051
		Enlisted Groundcrew	4.67	4.58	0.08 --	0.316
13-30	Triglycerides (mg/dl) [a]	All	107.4	105.6	1.8 --	0.546
		Officer	100.3	97.1	3.2 --	0.458
		Enlisted Flyer	107.0	119.5	–12.4 --	0.109
		Enlisted Groundcrew	110.5	105.2	5.3 --	0.239
13-32	Creatine Phosphokinase (U/l) [a]	All	140.3	139.4	0.9 --	0.809
		Officer	147.7	145.3	2.4 --	0.696
		Enlisted Flyer	131.5	136.4	–4.9 --	0.568
		Enlisted Groundcrew	140.2	138.3	1.8 --	0.736
13-34	Serum Amylase (U/l) [a]	All	63.65	63.74	–0.09 --	0.929
		Officer	61.86	65.36	–3.50 --	0.037
		Enlisted Flyer	65.17	62.44	2.73 --	0.301
		Enlisted Groundcrew	64.84	62.86	1.98 --	0.218
13-41	Prealbumin (mg/dl)	All	29.66	29.70	–0.04 (–0.47,0.39)	0.861
		Officer	30.03	30.20	–0.17 (–0.86,0.51)	0.621
		Enlisted Flyer	30.03	29.55	0.48 (–0.59,1.55)	0.382
		Enlisted Groundcrew	29.10	29.21	–0.11 (–0.76,0.54)	0.746
13-43	Albumin (mg/dl)	All	4,180.8	4,183.8	–3.0 (–32.1,26.0)	0.837
		Officer	4,163.1	4,192.1	–28.9 (–74.9,17.1)	0.218
		Enlisted Flyer	4,201.9	4,164.9	37.0 (–35.0,109.0)	0.314
		Enlisted Groundcrew	4,190.5	4,184.7	5.8 (–38.1,49.6)	0.797
13-45	α-1-Acid Glycoprotein (mg/dl) [a]	All	83.11	82.51	0.60 --	0.464
		Officer	78.64	80.08	–1.43 --	0.248
		Enlisted Flyer	83.83	83.68	0.15 --	0.942
		Enlisted Groundcrew	86.86	84.10	2.76 --	0.030
13-47	α-1-Antitrypsin (mg/dl) [c]	All	146.7	143.1	3.6 --	0.001
		Officer	138.6	137.9	0.7 --	0.693
		Enlisted Flyer	150.5	145.9	4.7 --	0.086
		Enlisted Groundcrew	151.5	145.6	5.9 --	<0.001
13-49	α-2-Macroglobulin (mg/dl) [a]	All	161.9	162.8	–0.9 --	0.610
		Officer	154.5	155.7	–1.2 --	0.643
		Enlisted Flyer	163.8	165.7	–1.9 --	0.664
		Enlisted Groundcrew	167.4	167.6	–0.2 --	0.951
13-51	Apolipoprotein B (mg/dl) [c]	All	110.6	111.8	–1.2 --	0.275
		Officer	105.9	109.2	–3.3 --	0.048
		Enlisted Flyer	112.9	115.1	–2.2 --	0.413
		Enlisted Groundcrew	112.6	111.4	1.2 --	0.457

Table G-13. Summary of Adjusted Results for Continuous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter (Units)	Occupational Category	Adj. Mean RH	Adj. Mean C	Difference of Adj. Means (95% C.I.)	p-Value
13-53	C3 Complement (mg/dl) [a]	All	120.2	120.0	0.2 --	0.837
		Officer	116.5	116.1	0.4 --	0.765
		Enlisted Flyer	120.8	122.2	–1.4 --	0.505
		Enlisted Groundcrew	122.8	122.3	0.6 --	0.668
13-55	C4 Complement (mg/dl) [a]	All	26.98	27.21	–0.23 --	0.333
		Officer	26.02	26.91	–0.90 --	0.017
		Enlisted Flyer	27.74	26.77	0.98 --	0.104
		Enlisted Groundcrew	27.61	27.67	–0.06 --	0.876
13-57	Haptoglobin (mg/dl) [c]	All	128.5	120.5	8.0 --	0.003
		Officer	112.2	106.8	5.4 --	0.172
		Enlisted Flyer	137.3	127.8	9.5 --	0.160
		Enlisted Groundcrew	137.4	127.4	9.9 --	0.016
13-59	Transferrin (mg/dl) [a]	All	246.2	243.1	3.1 --	0.037
		Officer	243.5	241.6	1.9 --	0.412
		Enlisted Flyer	247.9	244.8	3.1 --	0.404
		Enlisted Groundcrew	247.1	242.9	4.2 --	0.063
14-7	Systolic Blood Pressure (mm Hg) [a]	All	127.7	128.4	–0.6 --	0.415
		Officer	127.2	128.1	–0.9 --	0.468
		Enlisted Flyer	128.7	128.6	0.1 --	0.967
		Enlisted Groundcrew	127.5	128.2	–0.7 --	0.574
14-9	Diastolic Blood Pressure (mm Hg) [c]	All	75.68	75.62	0.06 --	0.889
		Officer	75.29	75.37	–0.08 --	0.907
		Enlisted Flyer	76.47	76.13	0.33 --	0.752
		Enlisted Groundcrew	75.37	75.29	0.08 --	0.898
15-3	RBC Count (million/mm^3)	All	4.95	4.96	–0.02 (–0.05,0.02)	0.311
		Officer	4.91	4.94	–0.03 (–0.08,0.02)	0.268
		Enlisted Flyer	4.94	4.98	–0.04 (–0.12,0.04)	0.343
		Enlisted Groundcrew	4.98	4.97	0.00 (–0.05,0.05)	0.919
15-5	WBC Count (thousand/mm^3) [a]	All	6.26	6.26	0.00 --	0.974
		Officer	6.03	6.03	0.00 --	0.972
		Enlisted Flyer	6.17	6.31	–0.14 --	0.377
		Enlisted Groundcrew	6.55	6.50	0.05 --	0.648
15-7	Hemoglobin (gm/dl)	All	15.05	15.05	–0.10 (–0.09,0.08)	0.883
		Officer	15.03	15.07	–0.05 (–0.18,0.09)	0.489
		Enlisted Flyer	15.02	15.10	–0.09 (–0.29,0.12)	0.422
		Enlisted Groundcrew	15.07	15.01	0.06 (–0.07,0.19)	0.356
15-9	Hematocrit (percent)	All	44.99	45.05	–0.06 (–0.32,0.21)	0.681
		Officer	44.90	45.11	–0.21 (–0.63,0.21)	0.326
		Enlisted Flyer	44.92	45.16	–0.24 (–0.88,0.41)	0.477
		Enlisted Groundcrew	45.08	44.93	0.15 (–0.25,0.55)	0.457
15-11	Platelet Count (thousand/mm^3) [c]	All	205.8	203.0	2.9 --	0.172
		Officer	199.1	207.3	–8.2 --	0.014
		Enlisted Flyer	213.3	197.7	15.6 --	0.003
		Enlisted Groundcrew	208.9	200.8	8.1 --	0.011

Table G-13. Summary of Adjusted Results for Continuous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter (Units)	Occupational Category	Adj. Mean RH	Adj. Mean C	Difference of Adj. Means (95% C.I.)	p-Value
15-13	Prothrombin Time (seconds) [a]	All	10.49	10.50	–0.01 --	0.873
		Officer	10.52	10.50	0.02 --	0.765
		Enlisted Flyer	10.45	10.48	–0.03 --	0.718
		Enlisted Groundcrew	10.50	10.51	–0.02 --	0.762
15-16	Absolute Neutrophils (segs) (thousand/mm^3) [a]	All	3.46	3.45	0.01 --	0.774
		Officer	3.26	3.28	–0.02 --	0.808
		Enlisted Flyer	3.44	3.47	–0.03 --	0.804
		Enlisted Groundcrew	3.68	3.61	0.06 --	0.416
15-17	Absolute Neutrophils (bands) (Nonzero Measurements) (thousand/mm^3) [a]	All	0.159	0.150	0.009 --	0.126
		Officer	0.152	0.141	0.011 --	0.221
		Enlisted Flyer	0.143	0.156	–0.013 --	0.389
		Enlisted Groundcrew	0.177	0.161	0.016 --	0.099
15-19	Absolute Lymphocytes (thousand/mm^3) [a]	All	1.79	1.79	0.00 --	0.964
		Officer	1.80	1.75	0.05 --	0.259
		Enlisted Flyer	1.74	1.82	–0.08 --	0.236
		Enlisted Groundcrew	1.82	1.83	–0.01 --	0.781
15-20	Absolute Monocytes (thousands/mm^3) [c]	All	0.471	0.476	–0.006 --	0.544
		Officer	0.461	0.468	–0.007 --	0.620
		Enlisted Flyer	0.452	0.490	–0.037 --	0.106
		Enlisted Groundcrew	0.489	0.481	0.008 --	0.590
15-21	Absolute Eosinophils (Nonzero Measurements) (thousand/mm^3) [a]	All	0.151	0.154	–0.003 --	0.576
		Officer	0.154	0.147	0.007 --	0.347
		Enlisted Flyer	0.150	0.153	–0.003 --	0.806
		Enlisted Groundcrew	0.149	0.162	–0.013 --	0.106
15-23	Absolute Basophils (Nonzero Measurements) (thousand/mm^3) [a]	All	0.072	0.074	–0.002 --	0.280
		Officer	0.071	0.073	–0.001 --	0.669
		Enlisted Flyer	0.072	0.074	–0.002 --	0.682
		Enlisted Groundcrew	0.073	0.076	–0.003 --	0.326
16-6	Time to Diabetes Onset (years)	All	--	--	--	0.871
		Officer	--	--	--	0.993
		Enlisted Flyer	--	--	--	0.390
		Enlisted Groundcrew	--	--	--	0.666
16-9	TSH (μIU/ml) [a]	All	1.64	1.57	0.07 --	0.105
		Officer	1.69	1.59	0.10 --	0.178
		Enlisted Flyer	1.48	1.58	–0.09 --	0.370
		Enlisted Groundcrew	1.71	1.60	0.11 --	0.088
16-11	Thyroxine (μg/dl) [c]	All	6.96	6.93	0.03 --	0.565
		Officer	6.58	6.66	–0.08 --	0.370
		Enlisted Flyer	7.12	7.08	0.04 --	0.774
		Enlisted Groundcrew	7.19	7.06	0.13 --	0.129
16-14	Fasting Glucose (mg/dl) [a]	All	103.7	103.8	0.0 --	0.970
		Officer	101.9	101.0	0.9 --	0.550
		Enlisted Flyer	104.1	105.7	–1.6 --	0.516
		Enlisted Groundcrew	104.7	105.1	–0.3 --	0.819

Table G-13. Summary of Adjusted Results for Continuous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter (Units)	Occupational Category	Adj. Mean RH	Adj. Mean C	Difference of Adj. Means (95% C.I.)	p-Value
16-16	2-Hour Postprandial Glucose (mg/dl) [a]	All	105.5	105.0	0.5 --	0.702
		Officer	103.0	99.5	3.5 --	0.086
		Enlisted Flyer	106.4	109.3	–2.9 --	0.405
		Enlisted Groundcrew	106.0	107.2	–1.2 --	0.563
16-20	Serum Insulin (μIU/ml) [a]	All	49.07	47.99	1.09 --	0.562
		Officer	43.72	41.32	2.40 --	0.353
		Enlisted Flyer	49.21	52.20	–2.99 --	0.548
		Enlisted Groundcrew	53.35	52.31	1.05 --	0.735
16-22	α-1-C Hemoglobin (percent) [a]	All	6.77	6.76	0.01 --	0.882
		Officer	6.61	6.55	0.06 --	0.427
		Enlisted Flyer	6.74	6.88	–0.14 --	0.284
		Enlisted Groundcrew	6.91	6.90	0.01 --	0.905
16-24	Total Testosterone (ng/dl) [c]	All	422.3	423.4	–1.1 --	0.883
		Officer	412.5	414.7	–2.2 --	0.848
		Enlisted Flyer	439.6	430.4	9.2 --	0.618
		Enlisted Groundcrew	418.5	422.2	–3.7 --	0.733
16-26	Free Testosterone (pg/ml) [c]	All	13.80	13.79	0.01 --	0.941
		Officer	13.39	13.61	–0.21 --	0.464
		Enlisted Flyer	14.23	14.10	0.13 --	0.783
		Enlisted Groundcrew	13.81	13.64	0.17 --	0.528
16-28	Estradiol (pg/ml) [c]	All	42.18	42.83	–0.65 --	0.384
		Officer	40.35	43.90	–3.55 --	0.003
		Enlisted Flyer	44.77	42.56	2.21 --	0.241
		Enlisted Groundcrew	42.26	41.37	0.89 --	0.427
16-30	LH (mIU/ml) [a]	All	3.84	3.85	–0.01 --	0.955
		Officer	3.85	3.63	0.22 --	0.185
		Enlisted Flyer	3.55	3.92	–0.37 --	0.147
		Enlisted Groundcrew	4.03	4.10	–0.08 --	0.650
16-32	FSH (mIU/ml) [a]	All	5.92	5.85	0.06 --	0.689
		Officer	6.01	5.62	0.40 --	0.112
		Enlisted Flyer	5.67	5.70	–0.03 --	0.928
		Enlisted Groundcrew	6.06	6.27	–0.21 --	0.401
17-4	CD3+ Cells (T Cells) (cells/mm^3) [a]	All	1,245.2	1,283.7	–38.5 --	0.255
		Officer	1,313.3	1,266.5	46.8 --	0.392
		Enlisted Flyer	1,201.6	1,298.4	–96.8 --	0.224
		Enlisted Groundcrew	1,205.6	1,297.3	–91.7 --	0.073
17-5	CD4+ Cells (Helper T Cells) (cells/mm^3) [a]	All	871.6	894.0	–22.4 --	0.333
		Officer	926.9	906.9	20.0 --	0.601
		Enlisted Flyer	835.6	896.5	–61.0 --	0.261
		Enlisted Groundcrew	842.4	886.4	–44.0 --	0.205
17-6	CD8+ Cells (Suppressor T Cells) (cells/mm^3) [a]	All	565.6	593.0	–27.4 --	0.169
		Officer	565.9	558.6	7.3 --	0.812
		Enlisted Flyer	551.8	624.3	–72.5 --	0.132
		Enlisted Groundcrew	564.7	606.9	–42.2 --	0.170

Table G-13. ***Summary of Adjusted Results for Continuous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)***

Table Ref.	Clinical Parameter (Units)	Occupational Category	Adj. Mean RH	Adj. Mean C	Difference of Adj. Means (95% C.I.)	p-Value
17-7	CD16+56+ Cells (Natural Killer Cells) (cells/mm³)[a]	All	265.8	281.6	−15.8 --	0.106
		Officer	261.0	271.7	−10.7 --	0.478
		Enlisted Flyer	241.8	300.4	−58.7 --	0.011
		Enlisted Groundcrew	280.8	283.3	−2.5 --	0.869
17-8	CD20+ Cells (B Cells) (cells/mm³)[a]	All	196.2	198.2	−2.0 --	0.808
		Officer	211.3	198.2	13.1 --	0.343
		Enlisted Flyer	185.0	199.7	−14.7 --	0.450
		Enlisted Groundcrew	189.2	199.3	−10.1 --	0.422
17-9	CD3+CD4+ Cells (Helper T Cells) (cells/mm³)[a]	All	786.5	807.2	−20.7 --	0.347
		Officer	839.6	820.0	19.6 --	0.589
		Enlisted Flyer	753.7	807.5	−53.8 --	0.296
		Enlisted Groundcrew	758.1	800.7	−42.5 --	0.196
17-10	Absolute Lymphocytes (cells/mm³)[a]	All	1,787.3	1,793.3	−6.1 --	0.827
		Officer	1,805.1	1,752.2	52.9 --	0.227
		Enlisted Flyer	1,740.1	1,814.4	−74.3 --	0.279
		Enlisted Groundcrew	1,795.4	1,830.0	−34.6 --	0.412
17-11	IgA (mg/dl)[a]	All	234.9	236.2	−1.4 --	0.790
		Officer	221.5	224.0	−2.5 --	0.740
		Enlisted Flyer	238.2	238.1	0.1 --	0.995
		Enlisted Groundcrew	246.1	246.8	−0.7 --	0.927
17-12	IgG (mg/dl)[a]	All	1,121.4	1,135.4	−13.9 --	0.217
		Officer	1,101.3	1,115.6	−14.3 --	0.417
		Enlisted Flyer	1,111.7	1,144.1	−32.3 --	0.251
		Enlisted Groundcrew	1,145.3	1,152.2	−6.8 --	0.694
17-13	IgM (mg/dl)[a]	All	90.5	92.4	−2.0 --	0.365
		Officer	89.2	89.9	−0.7 --	0.831
		Enlisted Flyer	89.3	98.1	−8.7 --	0.120
		Enlisted Groundcrew	90.7	91.4	−0.7 --	0.824
18-8	FVC (percent of predicted)	All	94.21	93.79	0.41 (−0.81.1.64)	0.506
		Officer	94.31	93.76	0.56 (−1.39,2.50)	0.575
		Enlisted Flyer	95.01	94.45	0.56 (−2.47,3.59)	0.716
		Enlisted Groundcrew	93.36	93.12	0.23 (−1.61,2.07)	0.804
18-9	FEV_1 (percent of predicted)	All	90.23	90.06	0.17 (−1.24,1.57)	0.814
		Officer	90.92	90.81	0.11 (−2.13,2.35)	0.925
		Enlisted Flyer	89.19	90.46	−1.27 (−4.75,2.21)	0.475
		Enlisted Groundcrew	90.07	89.32	0.75 (−1.36,2.87)	0.484
18-10	Ratio of Observed FEV_1 to Observed FVC[d]	All	0.770	0.771	−0.001 --	0.701
		Officer	0.771	0.775	−0.004 --	0.411
		Enlisted Flyer	0.764	0.770	−0.005 --	0.486
		Enlisted Groundcrew	0.774	0.771	0.003 --	0.532

[a] Means transformed from natural logarithm scale; difference of means after transformation to original scale; confidence interval not given because analysis was performed on natural logarithm scale; p-value based on difference of means on natural logarithm scale.

Table G-13. Summary of Adjusted Results for Continuous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

[b] Means transformed from natural logarithm (clinical parameter + 0.1) scale; difference of means after transformation to original scale; confidence interval not given because analysis was performed on natural logarithm (clinical parameter + 0.1) scale; p-value based on difference of means on natural logarithm (clinical parameter + 0.1) scale.
[c] Means transformed from square root scale; difference of means after transformation to original scale; confidence interval not given because analysis was performed on square root scale; p-value based on difference of means on square root scale.
[d] Means transformed from natural logarithm (1 – clinical parameter) scale; difference of means after transformation to original scale; confidence interval not given because analysis was performed on natural logarithm (1 – clinical parameter) scale; p-value based on difference of means on natural logarithm (1 – clinical parameter) scale.

Note: RH = Ranch Hand; C = Comparison.

Table G-14. Summary of Adjusted Results for Continuous Variables – Model 2 (Ranch Hands: Log_2 (Initial Dioxin))

Table Ref.	Clinical Parameter (Units)	R^2	Adj. Slope (Standard Error)	p-Value
9-6	Body Fat (percent) [a]	0.105	0.022 (0.010)	0.020
9-8	Erythrocyte Sedimentation Rate (mm/hr) [b]	0.086	0.041 (0.039)	0.289
10-35	PSA (ng/ml) [a]	0.114	–0.045 (0.031)	0.152
13-11	AST (U/l) [a]	0.057	0.010 (0.014)	0.493
13-13	ALT (U/l) [a]	0.094	0.011 (0.012)	0.357
13-15	GGT (U/l) [a]	0.097	0.008 (0.022)	0.709
13-17	Alkaline Phosphatase (U/l) [a]	0.037	–0.021 (0.011)	0.053
13-19	Total Bilirubin (mg/dl) [a]	0.038	0.004 (0.019)	0.822
13-22	Lactic Dehydrogenase (U/l) [a]	0.036	0.000 (0.007)	0.979
13-24	Cholesterol (mg/dl) [c]	0.044	0.083 (0.054)	0.122
13-26	HDL Cholesterol (mg/dl) [a]	0.132	0.005 (0.010)	0.625
13-28	Cholesterol-HDL Ratio [a]	0.118	0.007 (0.011)	0.499
13-30	Triglycerides (mg/dl) [a]	0.055	0.006 (0.027)	0.830
13-32	Creatine Phosphokinase (U/l) [a]	0.121	–0.004 (0.023)	0.871
13-34	Serum Amylase (U/l) [a]	0.125	–0.029 (0.015)	0.060
13-41	Prealbumin (mg/dl)	0.072	–0.127 (0.207)	0.538
13-43	Albumin (mg/dl)	0.054	–1.264 (12.791)	0.921
13-45	α-1-Acid Glycoprotein (mg/dl) [a]	0.046	–0.016 (0.009)	0.086
13-47	α-1-Antitrypsin (mg/dl) [c]	0.101	0.023 (0.041)	0.582
13-49	α-2-Macroglobulin (mg/dl) [a]	0.135	0.009 (0.010)	0.368
13-51	Apolipoprotein B (mg/dl) [c]	0.033	0.061 (0.048)	0.209
13-53	C3 Complement (mg/dl) [a]	0.083	0.009 (0.006)	0.145
13-55	C4 Complement (mg/dl) [a]	0.019	–0.004 (0.008)	0.638
13-57	Haptoglobin (mg/dl) [c]	0.066	–0.087 (0.111)	0.433
13-59	Transferrin (mg/dl) [a]	0.014	–0.001 (0.006)	0.798
14-7	Systolic Blood Pressure (mm Hg) [a]	0.135	–0.000 (0.006)	0.983
14-9	Diastolic Blood Pressure (mm Hg) [c]	0.073	0.019 (0.023)	0.425
15-3	RBC Count (million/mm^3)	0.070	–0.004 (0.016)	0.821
15-5	WBC Count (thousand/mm^3) [a]	0.213	0.008 (0.009)	0.414
15-7	Hemoglobin (gm/dl)	0.084	0.030 (0.039)	0.443
15-9	Hematocrit (percent)	0.068	0.091 (0.119)	0.443
15-11	Platelet Count (thousand/mm^3) [c]	0.090	0.073 (0.065)	0.262
15-13	Prothrombin Time (seconds) [a]	0.036	0.000 (0.003)	0.956
15-16	Absolute Neutrophils (segs) (thousand/mm^3) [a]	0.198	0.000 (0.012)	0.988
15-17	Absolute Neutrophils (bands) (Nonzero Measurements) (thousand/mm^3) [a]	0.117	–0.075 (0.036)	0.040
15-19	Absolute Lymphocytes (thousand/mm^3) [a]	0.064	0.024 (0.014)	0.087
15-20	Absolute Monocytes (thousand/mm^3) [c]	0.041	0.000 (0.006)	0.999
15-21	Absolute Eosinophils (Nonzero Measurements) (thousand/mm^3) [a]	0.009	0.012 (0.029)	0.670
15-23	Absolute Basophils (Nonzero Measurements) (thousand/mm^3) [a]	0.082	–0.003 (0.026)	0.917
16-6	Time to Diabetes Onset (years) [d]	--	–0.074 (0.030)	0.013
16-9	TSH (μIU/ml) [a]	0.071	–0.019 (0.024)	0.433
16-11	Thyroxine (μg/dl) [c]	0.045	–0.004 (0.010)	0.682
16-14	Fasting Glucose (mg/dl) [a]	0.160	0.023 (0.009)	0.014

Table G-14. Summary of Adjusted Results for Continuous Variables – Model 2 (Ranch Hands: Log_2 (Initial Dioxin)) (Continued)

Table Ref.	Clinical Parameter (Units)	R^2	Adj. Slope (Standard Error)	p-Value
16-16	2-Hour Postprandial Glucose (mg/dl) [a]	0.139	0.003 (0.013)	0.832
16-20	Serum Insulin (μIU/ml) [a]	0.195	0.054 (0.040)	0.170
16-22	α-1-C Hemoglobin (percent) [a]	0.163	0.024 (0.007)	0.001
16-24	Total Testosterone (ng/dl) [c]	0.206	–0.015 (0.161)	0.927
16-26	Free Testosterone (pg/ml) [c]	0.240	–0.008 (0.024)	0.742
16-28	Estradiol (pg/ml) [c]	0.019	0.046 (0.057)	0.423
16-30	LH (mIU/ml) [a]	0.014	–0.008 (0.027)	0.755
16-32	FSH (mIU/ml) [a]	0.051	–0.007 (0.024)	0.763
17-4	CD3+ Cells (T Cells) (cells/mm^3) [a]	0.132	0.042 (0.027)	0.113
17-5	CD4+ Cells (Helper T Cells) (cells/mm^3) [a]	0.152	0.041 (0.026)	0.119
17-6	CD8+ Cells (Suppressor T Cells) (cells/mm^3) [a]	0.039	0.023 (0.034)	0.505
17-7	CD16+56+ Cells (Natural Killer Cells) (cells/mm^3) [a]	0.112	–0.030 (0.038)	0.429
17-8	CD20+ Cells (B Cells) (cells/mm^3) [a]	0.236	0.075 (0.038)	0.052
17-9	CD3+CD4+ Cells (Helper T Cells) (cells/mm^3) [a]	0.159	0.046 (0.028)	0.098
17-10	Absolute Lymphocytes (cells/mm^3) [a]	0.066	0.023 (0.014)	0.109
17-11	IgA (mg/dl) [a]	0.049	0.040 (0.020)	0.046
17-12	IgG (mg/dl) [a]	0.119	–0.003 (0.010)	0.761
17-13	IgM (mg/dl) [a]	0.046	–0.003 (0.022)	0.896
18-8	FVC (percent of predicted)	0.099	–0.303 (0.558)	0.588
18-9	FEV_1 (percent of predicted)	0.143	0.007 (0.637)	0.991
18-10	Ratio of Observed FEV_1 to Observed FVC [e]	0.216	–0.011 (0.012)	0.360

[a] Slope and standard error based on natural logarithm of clinical parameter versus $\log_2$ (initial dioxin).
[b] Slope and standard error based on natural logarithm of (clinical parameter + 0.1) versus $\log_2$ (initial dioxin).
[c] Slope and standard error based on square root of clinical parameter versus $\log_2$ (initial dioxin).
[d] Slope and standard error based on time to diabetes onset versus $\log_2$ (initial dioxin) under a censored Weibull distribution.
[e] Slope and standard error based on natural logarithm of (1 – clinical parameter) versus $\log_2$ (initial dioxin).
--: R-squared not presented because analysis was based on a censored Weibull distribution.

Table G-15. Summary of Adjusted Results for Continuous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category)

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Adj. Mean	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
9-6	Body Fat (percent) [a]	0.069	Comparison	1,211	22.25		
			Background RH	378	20.73	–1.52 --	<0.001
			Low RH	237	23.00	0.75 --	0.052
			High RH	241	23.51	1.26 --	0.002
			Low plus High RH	478	23.26	1.01 --	0.001
9-8	Erythrocyte Sedimentation Rate (mm/hr) [b]	0.083	Comparison	1,211	5.12		
			Background RH	376	4.92	–0.20 --	0.484
			Low RH	237	5.12	0.00 --	0.992
			High RH	240	5.48	0.36 --	0.322
			Low plus High RH	477	5.29	0.17 --	0.510
10-35	PSA (ng/ml) [a]	0.085	Comparison	1,151	1.201		
			Background RH	362	1.163	–0.038 --	0.527
			Low RH	221	1.258	0.057 --	0.441
			High RH	234	1.209	0.008 --	0.919
			Low plus High RH	455	1.232	0.031 --	0.600
13-11	AST (U/l) [a]	0.033	Comparison	1,193	23.23		
			Background RH	374	22.76	–0.47 --	0.305
			Low RH	235	23.93	0.70 --	0.207
			High RH	238	24.17	0.94 --	0.100
			Low plus High RH	473	24.05	0.82 --	0.055
13-13	ALT (U/l) [a]	0.093	Comparison	1,193	42.21		
			Background RH	374	41.31	–0.90 --	0.192
			Low RH	235	43.65	1.44 --	0.084
			High RH	238	43.62	1.41 --	0.098
			Low plus High RH	473	43.63	1.42 --	0.026

Table G-15. Summary of Adjusted Results for Continuous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Adj. Mean	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
13-15	GGT (U/l) [a]	0.115	Comparison	1,193	45.40		
			Background RH	374	44.67	–0.73 --	0.606
			Low RH	235	47.84	2.43 --	0.159
			High RH	238	50.40	5.00 --	0.006
			Low plus High RH	473	49.11	3.71 --	0.006
13-17	Alkaline Phosphatase (U/l) [a]	0.027	Comparison	1,193	80.38		
			Background RH	375	83.68	3.48 --	0.008
			Low RH	235	83.18	2.79 --	0.071
			High RH	239	80.32	–0.06 --	0.967
			Low plus High RH	474	81.72	1.34 --	0.255
13-19	Total Bilirubin (mg/dl) [a]	0.022	Comparison	1,193			
			Background RH	374	0.517	–0.002 --	0.901
			Low RH	235	0.515	–0.003 --	0.884
			High RH	238	0.520	0.003 --	0.861
			Low plus High RH	473	0.517	0.000 --	0.981
13-22	Lactic Dehydrogenase (U/l) [a]	0.036	Comparison	1,192	155.5		
			Background RH	374	156.1	0.6 --	0.737
			Low RH	235	155.0	–0.5 --	0.774
			High RH	238	156.8	1.3 --	0.528
			Low plus High RH	473	155.9	0.4 --	0.812
13-24	Cholesterol (mg/dl) [c]	0.018	Comparison	1,193	212.9		
			Background RH	374	211.0	–1.9 --	0.392
			Low RH	235	210.6	–2.3 --	0.389
			High RH	238	217.3	4.4 --	0.115
			Low plus High RH	473	214.0	1.1 --	0.616
13-26	HDL Cholesterol (mg/dl) [a]	0.116	Comparison	1,192	46.77		
			Background RH	374	47.11	0.34 --	0.628
			Low RH	234	47.10	0.33 --	0.687
			High RH	238	46.77	0.00 --	0.999
			Low plus High RH	472	46.93	0.16 --	0.795

Table G-15. Summary of Adjusted Results for Continuous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Adj. Mean	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
13-28	Cholesterol-HDL Ratio [a]	0.088	Comparison	1,192	4.52		
			Background RH	374	4.45	–0.07 --	0.352
			Low RH	234	4.43	–0.09 --	0.289
			High RH	238	4.61	0.09 --	0.290
			Low plus High RH	472	4.52	0.00 --	0.978
13-30	Triglycerides (mg/dl) [a]	0.082	Comparison	1,193	105.9		
			Background RH	373	103.2	–2.7 --	0.483
			Low RH	235	107.0	1.1 --	0.820
			High RH	238	118.2	12.3 --	0.013
			Low plus High RH	473	112.5	6.6 --	0.070
13-32	Creatine Phosphokinase (U/l) [a]	0.102	Comparison	1,193	140.2		
			Background RH	374	139.5	–0.7 --	0.889
			Low RH	235	142.6	2.4 --	0.679
			High RH	238	143.8	3.6 --	0.549
			Low plus High RH	473	143.2	3.0 --	0.503
13-34	Serum Amylase (U/l) [a]	0.075	Comparison	1,193	63.45		
			Background RH	374	62.33	–1.12 --	0.427
			Low RH	235	66.45	3.00 --	0.078
			High RH	238	61.31	–2.14 --	0.205
			Low plus High RH	473	63.82	0.37 --	0.774
13-41	Prealbumin (mg/dl)	0.055	Comparison	1,193	29.65		
			Background RH	374	29.51	–0.15 (–0.73,0.44)	0.626
			Low RH	235	29.69	0.04 (–0.65,0.73)	0.908
			High RH	238	29.72	0.06 (–0.64,0.77)	0.860
			Low plus High RH	473	29.71	0.05 (–0.48,0.58)	0.847

Table G-15. Summary of Adjusted Results for Continuous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Adj. Mean	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
13-43	Albumin (mg/dl)	0.042	Comparison	1,193	4,183.0		
			Background RH	374	4,187.9	5.0 (–34.0,43.9)	0.803
			Low RH	235	4,154.2	–28.7 (–74.7,17.3)	0.221
			High RH	238	4,200.2	17.2 (–30.0,64.4)	0.476
			Low plus High RH	473	4,177.3	–5.6 (–41.0,29.8)	0.755
13-45	α-1-Acid Glycoprotein (mg/dl) [a]	0.029	Comparison	1,193	82.72		
			Background RH	374	82.67	–0.05 --	0.961
			Low RH	235	83.42	0.70 --	0.600
			High RH	238	83.78	1.06 --	0.436
			Low plus High RH	473	83.60	0.88 --	0.389
13-47	α-1-Antitrypsin (mg/dl) [c]	0.062	Comparison	1,193	143.8		
			Background RH	374	147.2	3.4 --	0.024
			Low RH	235	145.5	1.7 --	0.339
			High RH	238	148.4	4.6 --	0.011
			Low plus High RH	473	147.0	3.2 --	0.020
13-49	α-2-Macroglobulin (mg/dl) [a]	0.113	Comparison	1,193	163.2		
			Background RH	374	162.2	–1.0 --	0.683
			Low RH	235	159.9	–3.3 --	0.232
			High RH	238	163.3	0.1 --	0.959
			Low plus High RH	473	161.6	–1.6 --	0.461
13-51	Apolipoprotein B (mg/dl) [c]	0.015	Comparison	1,193	112.0		
			Background RH	374	110.0	–2.0 --	0.170
			Low RH	235	109.5	–2.5 --	0.154
			High RH	238	113.6	1.6 --	0.358
			Low plus High RH	473	111.6	–0.4 --	0.761
13-53	C3 Complement (mg/dl) [a]	0.126	Comparison	1,193	120.1		
			Background RH	374	119.5	–0.6 --	0.594
			Low RH	235	121.0	0.9 --	0.518
			High RH	238	121.8	1.7 --	0.217
			Low plus High RH	473	121.4	1.3 --	0.213

Table G-15. Summary of Adjusted Results for Continuous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Adj. Mean	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
13-55	C4 Complement (mg/dl) [a]	0.039	Comparison	1,193	27.24		
			Background RH	374	26.93	–0.31 --	0.336
			Low RH	235	27.27	0.03 --	0.942
			High RH	238	26.97	–0.27 --	0.494
			Low plus High RH	473	27.12	–0.12 --	0.680
13-57	Haptoglobin (mg/dl) [c]	0.044	Comparison	1,193	120.9		
			Background RH	374	129.8	8.9 --	0.014
			Low RH	235	127.5	6.6 --	0.118
			High RH	238	128.0	7.1 --	0.105
			Low plus High RH	473	127.7	6.8 --	0.036
13-59	Transferrin (mg/dl) [a]	0.021	Comparison	1,193	243.0		
			Background RH	374	245.2	2.2 --	0.282
			Low RH	235	246.1	3.1 --	0.200
			High RH	238	247.9	4.9 --	0.050
			Low plus High RH	473	247.0	4.0 --	0.032
14-7	Systolic Blood Pressure (mm Hg) [a]	0.109	Comparison	1,155	128.5		
			Background RH	360	128.5	0.0 --	0.990
			Low RH	221	127.9	–0.6 --	0.651
			High RH	236	127.0	–1.5 --	0.222
			Low plus High RH	457	127.4	–1.1 --	0.262
14-9	Diastolic Blood Pressure (mm Hg) [c]	0.050	Comparison	1,155	75.67		
			Background RH	360	75.56	–0.11 --	0.844
			Low RH	221	75.23	–0.44 --	0.515
			High RH	236	76.69	1.02 --	0.135
			Low plus High RH	457	75.98	0.31 --	0.544
15-3	RBC Count (million/mm^3)	0.052	Comparison	1,210	4.97		
			Background RH	380	4.97	0.00 (–0.04,0.05)	0.893
			Low RH	238	4.93	–0.03 (–0.09,0.02)	0.230
			High RH	239	4.94	–0.02 (–0.08,0.03)	0.441
			Low plus High RH	477	4.94	–0.03 (–0.07,0.01)	0.196

Table G-15. Summary of Adjusted Results for Continuous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Adj. Mean	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
15-5	WBC Count (thousand/mm^3) [a]	0.206	Comparison	1,210	6.27		
			Background RH	380	6.28	0.01 --	0.902
			Low RH	238	6.18	–0.09 --	0.383
			High RH	239	6.33	0.06 --	0.600
			Low plus High RH	477	6.26	–0.01 --	0.831
15-7	Hemoglobin (gm/dl)	0.086	Comparison	1,210	15.06		
			Background RH	380	15.04	–0.02 (–0.14,0.09)	0.679
			Low RH	238	15.04	–0.02 (–0.16,0.11)	0.731
			High RH	239	15.12	0.06 (–0.08,0.20)	0.379
			Low plus High RH	477	15.08	0.02 (–0.08,0.12)	0.715
15-9	Hematocrit (percent)	0.067	Comparison	1,210	45.08		
			Background RH	380	45.04	–0.04 (–0.39,0.32)	0.839
			Low RH	238	44.87	–0.21 (–0.63,0.20)	0.318
			High RH	239	45.22	0.14 (–0.29,0.56)	0.534
			Low plus High RH	477	45.04	–0.04 (–0.36,0.28)	0.817
15-11	Platelet Count (thousand/mm^3) [c]	0.041	Comparison	1,204	204.2		
			Background RH	378	202.3	–1.9 --	0.509
			Low RH	237	204.4	0.2 --	0.959
			High RH	238	214.8	10.6 --	0.002
			Low plus High RH	475	209.6	5.4 --	0.038
15-13	Prothrombin Time (seconds) [a]	0.012	Comparison	986	10.50		
			Background RH	308	10.52	0.02 --	0.695
			Low RH	182	10.46	–0.04 --	0.521
			High RH	193	10.49	–0.01 --	0.823
			Low plus High RH	375	10.47	–0.03 --	0.575

Table G-15. Summary of Adjusted Results for Continuous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Adj. Mean	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
15-16	Absolute Neutrophils (segs) (thousand/mm^3)[a]	0.171	Comparison	1,210	3.45		
			Background RH	380	3.45	0.00 --	0.961
			Low RH	238	3.44	–0.01 --	0.854
			High RH	239	3.50	0.05 --	0.551
			Low plus High RH	477	3.47	0.02 --	0.780
15-17	Absolute Neutrophils (bands) (Nonzero Measurements) (thousand/mm^3)[a]	0.078	Comparison	1,001	0.148		
			Background RH	315	0.150	0.002 --	0.750
			Low RH	195	0.165	0.017 --	0.076
			High RH	201	0.161	0.013 --	0.166
			Low plus High RH	396	0.163	0.015 --	0.038
15-19	Absolute Lymphocytes (thousand/mm^3)[a]	0.060	Comparison	1,210	1.79		
			Background RH	380	1.83	0.04 --	0.356
			Low RH	238	1.77	–0.02 --	0.572
			High RH	239	1.77	–0.02 --	0.572
			Low plus High RH	477	1.77	–0.02 --	0.457
15-20	Absolute Monocytes (thousand/mm^3)[c]	0.050	Comparison	1,210	0.479		
			Background RH	380	0.464	–0.015 --	0.223
			Low RH	238	0.464	–0.015 --	0.319
			High RH	239	0.499	0.020 --	0.193
			Low plus High RH	477	0.482	0.003 --	0.822
15-21	Absolute Eosinophils (Nonzero Measurements) (thousand/mm^3)[a]	0.025	Comparison	1,063	0.153		
			Background RH	336	0.156	0.003 --	0.677
			Low RH	205	0.147	–0.006 --	0.447
			High RH	211	0.144	–0.009 --	0.229
			Low plus High RH	416	0.146	–0.007 --	0.194
15-23	Absolute Basophils (Nonzero Measurements) (thousand/mm^3)[a]	0.088	Comparison	562	0.075		
			Background RH	168	0.074	–0.001 --	0.657
			Low RH	91	0.071	–0.004 --	0.183
			High RH	109	0.073	–0.002 --	0.563
			Low plus High RH	200	0.072	–0.003 --	0.220

Table G-15. Summary of Adjusted Results for Continuous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Adj. Mean	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
16-6	Time to Diabetes Onset (years)	--	Comparison	1,183	--		
			Background RH	375	--	--	0.024
			Low RH	232	--	--	0.214
			High RH	238	--	--	0.100
			Low plus High RH	470	--	--	0.061
16-9	TSH (μIU/ml) [a]	0.033	Comparison	1,161	1.57		
			Background RH	365	1.64	0.07 --	0.250
			Low RH	233	1.64	0.07 --	0.292
			High RH	233	1.62	0.05 --	0.454
			Low plus High RH	466	1.63	0.06 --	0.237
16-11	Thyroxine (μg/dl) [c]	0.031	Comparison	1,161	6.93		
			Background RH	365	6.93	0.00 --	0.969
			Low RH	233	7.02	0.09 --	0.344
			High RH	233	6.98	0.05 --	0.646
			Low plus High RH	466	7.00	0.07 --	0.357
16-14	Fasting Glucose (mg/dl) [a]	0.132	Comparison	1,200	103.8		
			Background RH	377	102.8	–1.0 --	0.418
			Low RH	235	102.9	–0.9 --	0.551
			High RH	240	106.3	2.5 --	0.106
			Low plus High RH	475	104.6	0.8 --	0.482
16-16	2-Hour Postprandial Glucose (mg/dl) [a]	0.116	Comparison	987	105.1		
			Background RH	338	106.1	1.0 --	0.585
			Low RH	183	106.1	1.0 --	0.655
			High RH	181	104.6	–0.5 --	0.804
			Low plus High RH	364	105.4	0.3 --	0.900

Table G-15. Summary of Adjusted Results for Continuous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Adj. Mean	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
16-20	Serum Insulin (μIU/ml)[a]	0.208	Comparison	987	47.57		
			Background RH	338	47.31	–0.26 --	0.914
			Low RH	183	49.87	2.30 --	0.455
			High RH	181	51.51	3.94 --	0.226
			Low plus High RH	364	50.68	3.11 --	0.195
16-22	α-1-C Hemoglobin (percent)[a]	0.136	Comparison	1,200	6.78		
			Background RH	377	6.72	–0.06 --	0.412
			Low RH	235	6.70	–0.08 --	0.330
			High RH	240	6.97	0.19 --	0.022
			Low plus High RH	475	6.83	0.05 --	0.363
16-24	Total Testosterone (ng/dl)[c]	0.169	Comparison	1,189	422.9		
			Background RH	370	434.4	11.5 --	0.248
			Low RH	234	414.5	–8.4 --	0.470
			High RH	237	416.8	–6.1 --	0.613
			Low plus High RH	471	415.7	–7.2 --	0.420
16-26	Free Testosterone (pg/ml)[c]	0.220	Comparison	1,189	13.80		
			Background RH	370	13.98	0.18 --	0.459
			Low RH	234	13.50	–0.30 --	0.315
			High RH	237	13.94	0.14 --	0.643
			Low plus High RH	471	13.72	–0.08 --	0.735
16-28	Estradiol (pg/ml)[c]	0.009	Comparison	1,213	42.96		
			Background RH	381	41.76	–1.20 --	0.241
			Low RH	239	41.51	–1.45 --	0.231
			High RH	243	44.13	1.17 --	0.374
			Low plus High RH	482	42.82	–0.14 --	0.888

Table G-15. Summary of Adjusted Results for Continuous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Adj. Mean	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
16-30	LH (mIU/ml) [a]	0.047	Comparison	1,213	3.84		
			Background RH	381	4.00	0.16 --	0.281
			Low RH	239	3.73	–0.11 --	0.479
			High RH	243	3.81	–0.03 --	0.839
			Low plus High RH	482	3.77	–0.07 --	0.553
16-32	FSH (mIU/ml) [a]	0.072	Comparison	1,213	5.87		
			Background RH	381	6.02	0.15 --	0.491
			Low RH	239	5.98	0.11 --	0.668
			High RH	243	5.83	–0.04 --	0.855
			Low plus High RH	482	5.90	0.03 --	0.877
17-4	CD3+ Cells (T Cells) (cells/mm^3) [a]	0.096	Comparison	436	1,284.8		
			Background RH	140	1,237.1	–47.7 --	0.308
			Low RH	83	1,272.3	–12.5 --	0.823
			High RH	91	1,239.1	–45.5 --	0.403
			Low plus High RH	174	1,254.9	–29.9 --	0.474
17-5	CD4+ Cells (Helper T Cells) (cells/mm^3) [a]	0.116	Comparison	436	897.9		
			Background RH	140	854.8	–43.1 --	0.176
			Low RH	83	893.6	–4.3 --	0.911
			High RH	91	886.1	–11.8 --	0.752
			Low plus High RH	174	889.7	–8.2 --	0.774
17-6	CD8+ Cells (Suppressor T Cells) (cells/mm^3) [a]	0.040	Comparison	436	592.0		
			Background RH	140	576.2	–15.8 --	0.574
			Low RH	83	576.2	–15.8 --	0.634
			High RH	91	541.9	–50.1 --	0.112
			Low plus High RH	174	558.0	–34.0 --	0.164
17-7	CD16+56+ Cells (Natural Killer Cells) (cells/mm^3) [a]	0.051	Comparison	436	282.6		
			Background RH	140	268.0	–14.6 --	0.285
			Low RH	83	286.7	4.1 --	0.805
			High RH	91	252.0	–30.6 --	0.046
			Low plus High RH	174	268.0	–14.6 --	0.227

Table G-15. Summary of Adjusted Results for Continuous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Adj. Mean	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
17-8	CD20+ Cells (B Cells) (cells/mm^3) [a]	0.111	Comparison	436	198.1		
			Background RH	140	200.6	2.5 --	0.827
			Low RH	82	185.2	−12.9 --	0.325
			High RH	91	194.6	−3.5 --	0.788
			Low plus High RH	173	190.1	−8.0 --	0.419
17-9	CD3+CD4+ Cells (Helper T Cells) (cells/mm^3) [a]	0.122	Comparison	436	809.9		
			Background RH	140	766.6	−43.3 --	0.151
			Low RH	82	806.9	−3.0 --	0.935
			High RH	91	803.8	−6.1 --	0.865
			Low plus High RH	174	805.3	−4.6 --	0.866
17-10	Absolute Lymphocytes (cells/mm^3) [a]	0.060	Comparison	1,154	1,794.7		
			Background RH	365	1,821.6	26.9 --	0.477
			Low RH	220	1,768.7	−26.0 --	0.562
			High RH	229	1,755.8	−38.9 --	0.389
			Low plus High RH	449	1,762.1	−32.6 --	0.340
17-11	IgA (mg/dl) [a]	0.018	Comparison	1,154	236.3		
			Background RH	365	231.0	−5.3 --	0.435
			Low RH	220	233.2	−3.1 --	0.707
			High RH	229	241.0	4.7 --	0.575
			Low plus High RH	449	237.1	0.8 --	0.890
17-12	IgG (mg/dl) [a]	0.070	Comparison	1,154	1,136.6		
			Background RH	365	1,122.1	−14.5 --	0.340
			Low RH	220	1,121.4	−15.2 --	0.404
			High RH	229	1,125.1	−11.5 --	0.535
			Low plus High RH	449	1,123.3	−13.3 --	0.340

Table G-15. Summary of Adjusted Results for Continuous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Adj. Mean	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
17-13	IgM (mg/dl) [a]	0.019	Comparison	1,154	92.5		
			Background RH	365	91.2	–1.3 --	0.659
			Low RH	220	90.7	–1.8 --	0.599
			High RH	229	89.4	–3.1 --	0.390
			Low plus High RH	449	90.0	–2.5 --	0.358
18-8	FVC (percent of predicted)	0.119	Comparison	1,210	93.87		
			Background RH	380	93.72	–0.15 (–1.80,1.50)	0.859
			Low RH	237	94.29	0.42 (–1.54,2.39)	0.674
			High RH	243	94.61	0.75 (–1.25,2.74)	0.465
			Low plus High RH	480	94.45	0.59 (–0.92,2.09)	0.445
18-9	FEV_1 (percent of predicted)	0.153	Comparison	1,210	90.03		
			Background RH	380	89.32	–0.70 (–2.59,1.19)	0.469
			Low RH	237	90.58	0.55 (–1.70,2.80)	0.632
			High RH	243	91.19	1.16 (–1.13,3.45)	0.319
			Low plus High RH	480	90.89	0.86 (–0.86,2.58)	0.328
18-10	Ratio of Observed FEV_1 to Observed FVC [d]	0.195	Comparison	1,210	0.770		
			Background RH	380	0.766	–0.004 --	0.376
			Low RH	237	0.772	0.002 --	0.740
			High RH	243	0.774	0.004 --	0.466
			Low plus High RH	480	0.773	0.003 --	0.481

[a] Means transformed from natural logarithm scale; difference of means after transformation to original scale; confidence interval not given because analysis was performed on natural logarithm scale; p-value based on difference of means on natural logarithm scale.

[b] Means transformed from natural logarithm (clinical parameter + 0.1) scale; difference of means after transformation to original scale; confidence interval not given because analysis was performed on natural logarithm (clinical parameter + 0.1) scale; p-value based on difference of means on natural logarithm (clinical parameter + 0.1) scale.

[c] Means transformed from square root scale; difference of means after transformation to original scale; confidence interval not given because analysis was performed on square root scale; p-value based on difference of means on square root scale.

[d] Means transformed from natural logarithm (1 – clinical parameter) scale; difference of means after transformation to original scale; confidence interval not given because analysis was performed on natural logarithm (1 – clinical parameter) scale; p-value based on difference of means on natural logarithm (1 – clinical parameter) scale.

Table G-15. Summary of Adjusted Results for Continuous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background: (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table G-16. Summary of Adjusted Results for Continuous Variables – Model 4 (Ranch Hands: Log_2 (1987 Dioxin + 1))

Table Ref.	Clinical Parameter (Units)	R^2	Adj. Slope (Standard Error)	p-Value
9-6	Body Fat (percent) [a]	0.155	0.054 (0.006)	<0.001
9-8	Erythrocyte Sedimentation Rate (mm/hr) [b]	0.088	0.052 (0.025)	0.037
10-35	PSA (ng/ml) [a]	0.076	–0.021 (0.020)	0.312
13-11	AST (U/l) [a]	0.036	0.028 (0.009)	0.002
13-13	ALT (U/l) [a]	0.079	0.033 (0.007)	<0.001
13-15	GGT (U/l) [a]	0.103	0.042 (0.014)	0.003
13-17	Alkaline Phosphatase (U/l) [a]	0.042	–0.021 (0.007)	0.003
13-19	Total Bilirubin (mg/dl) [a]	0.023	0.008 (0.012)	0.519
13-22	Lactic Dehydrogenase (U/l) [a]	0.015	0.006 (0.005)	0.187
13-24	Cholesterol (mg/dl) [c]	0.023	0.046 (0.034)	0.178
13-26	HDL Cholesterol (mg/dl) [a]	0.081	–0.014 (0.007)	0.037
13-28	Cholesterol-HDL Ratio [a]	0.074	0.021 (0.007)	0.006
13-30	Triglycerides (mg/dl) [a]	0.041	0.063 (0.017)	<0.001
13-32	Creatine Phosphokinase (U/l) [a]	0.091	0.039 (0.015)	0.011
13-34	Serum Amylase (U/l) [a]	0.063	–0.030 (0.010)	0.003
13-41	Prealbumin (mg/dl)	0.053	–0.007 (0.140)	0.961
13-43	Albumin (mg/dl)	0.040	–11.121 (8.711)	0.202
13-45	α-1-Acid Glycoprotein (mg/dl) [a]	0.056	–0.012 (0.006)	0.049
13-47	α-1-Antitrypsin (mg/dl) [c]	0.102	–0.047 (0.027)	0.089
13-49	α-2-Macroglobulin (mg/dl) [a]	0.131	–0.005 (0.006)	0.390
13-51	Apolipoprotein B (mg/dl) [c]	0.023	0.046 (0.031)	0.142
13-53	C3 Complement (mg/dl) [a]	0.067	0.017 (0.004)	<0.001
13-55	C4 Complement (mg/dl) [a]	0.044	0.001 (0.005)	0.849
13-57	Haptoglobin (mg/dl) [c]	0.055	–0.116 (0.073)	0.114
13-59	Transferrin (mg/dl) [a]	0.014	0.003 (0.004)	0.385
14-7	Systolic Blood Pressure (mm Hg) [a]	0.126	–0.005 (0.004)	0.165
14-9	Diastolic Blood Pressure (mm Hg) [c]	0.061	0.016 (0.016)	0.315
15-3	RBC Count (million/mm^3)	0.047	–0.001 (0.010)	0.941
15-5	WBC Count (thousand/mm^3) [a]	0.219	0.007 (0.006)	0.263
15-7	Hemoglobin (gm/dl)	0.088	0.021 (0.026)	0.421
15-9	Hematocrit (percent)	0.075	0.029 (0.079)	0.712
15-11	Platelet Count (thousand/mm^3) [c]	0.066	0.049 (0.044)	0.264
15-13	Prothrombin Time (seconds) [a]	0.016	–0.001 (0.002)	0.685
15-16	Absolute Neutrophils (segs) (thousand/mm^3) [a]	0.196	0.006 (0.008)	0.455
15-17	Absolute Neutrophils (bands) (Nonzero Measurements) (thousand/mm^3) [a]	0.076	0.011 (0.024)	0.657
15-19	Absolute Lymphocytes (thousand/mm^3) [a]	0.050	0.007 (0.009)	0.455
15-20	Absolute Monocytes (thousand/mm^3) [c]	0.032	0.007 (0.004)	0.125
15-21	Absolute Eosinophils (Nonzero Measurements) (thousand/mm^3) [a]	0.028	–0.010 (0.020)	0.608
15-23	Absolute Basophils (Nonzero Measurements) (thousand/mm^3) [a]	0.076	–0.006 (0.016)	0.716
16-6	Time to Diabetes Onset (years) [d]	--	–0.118 (0.027)	<0.001
16-9	TSH (μIU/ml) [a]	0.046	0.008 (0.017)	0.624
16-11	Thyroxine (μg/dl) [c]	0.047	–0.001 (0.007)	0.862
16-14	Fasting Glucose (mg/dl) [a]	0.082	0.018 (0.006)	0.002

Table G-16. Summary of Adjusted Results for Continuous Variables – Model 4 (Ranch Hands: Log_2 (Initial Dioxin + 1))(Continued)

Table Ref.	Clinical Parameter (Units)	R^2	Adj. Slope (Standard Error)	p-Value
16-16	2-Hour Postprandial Glucose (mg/dl) [a]	0.137	0.002 (0.008)	0.850
16-20	Serum Insulin (μIU/ml) [a]	0.235	0.026 (0.025)	0.305
16-22	α-1-C Hemoglobin (percent) [a]	0.119	0.016 (0.005)	<0.001
16-24	Total Testosterone (ng/dl) [c]	0.193	–0.149 (0.109)	0.172
16-26	Free Testosterone (pg/ml) [c]	0.234	–0.029 (0.016)	0.066
16-28	Estradiol (pg/ml) [c]	0.017	0.019 (0.036)	0.599
16-30	LH (mIU/ml) [a]	0.034	–0.024 (0.017)	0.149
16-32	FSH (mIU/ml) [a]	0.066	–0.001 (0.016)	0.958
17-4	CD3+ Cells (T Cells) (cells/mm^3) [a]	0.088	0.035 (0.018)	0.046
17-5	CD4+ Cells (Helper T Cells) (cells/mm^3) [a]	0.091	0.038 (0.018)	0.033
17-6	CD8+ Cells (Suppressor T Cells) (cells/mm^3) [a]	0.049	0.014 (0.022)	0.540
17-7	CD16+56+ Cells (Natural Killer Cells) (cells/mm^3) [a]	0.059	–0.001 (0.025)	0.960
17-8	CD20+ Cells (B Cells) (cells/mm^3) [a]	0.105	0.030 (0.026)	0.253
17-9	CD3+CD4+ Cells (Helper T Cells) (cells/mm^3) [a]	0.097	0.042 (0.019)	0.025
17-10	Absolute Lymphocytes (cells/mm^3) [a]	0.046	0.008 (0.009)	0.393
17-11	IgA (mg/dl) [a]	0.031	0.021 (0.013)	0.115
17-12	IgG (mg/dl) [a]	0.073	–0.001 (0.006)	0.920
17-13	IgM (mg/dl) [a]	0.025	–0.008 (0.014)	0.586
18-8	FVC (percent of predicted)	0.111	0.377 (0.385)	0.329
18-9	FEV_1 (percent of predicted)	0.161	0.652 (0.443)	0.142
18-10	Ratio of Observed FEV_1 to Observed FVC [e]	0.218	–0.012 (0.008)	0.161

[a] Slope and standard error based on natural logarithm of clinical parameter versus log_2 (initial dioxin).
[b] Slope and standard error based on natural logarithm of (clinical parameter + 0.1) versus log_2 (initial dioxin).
[c] Slope and standard error based on square root of clinical parameter versus log_2 (initial dioxin).
[d] Slope and standard error based on time to diabetes onset versus log_2 (initial dioxin) under a censored Weibull distribution.
[e] Slope and standard error based on natural logarithm of (1 – clinical parameter) versus log_2 (initial dioxin).
--: R-squared not presented because analysis was based on a censored Weibull distribution.

Table G-17. Summary of Adjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons)

Table Ref.	Clinical Parameter	Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value
9-3	Self-perception of Health	All	1.43 (1.09,1.87)	0.010
		Officer	1.26 (0.75,2.12)	0.383
		Enlisted Flyer	1.52 (0.82,2.82)	0.183
		Enlisted Groundcrew	1.48 (1.03,2.14)	0.035
9-4	Appearance of Illness or Distress	All	1.44 (0.67,3.06)	0.350
		Officer	1.13 (0.25,5.16)	0.878
		Enlisted Flyer	2.12 (0.33,13.61)	0.426
		Enlisted Groundcrew	1.42 (0.52,3.89)	0.496
9-5	Relative Age Appearance	All	1.21 (0.88,1.65)	0.237
		Officer	1.29 (0.70,2.36)	0.410
		Enlisted Flyer	1.28 (0.65,2.50)	0.476
		Enlisted Groundcrew	1.14 (0.74,1.75)	0.550
9-7	Body Fat	All	0.92 (0.75,1.11)	0.369
		Officer	1.05 (0.77,1.45)	0.754
		Enlisted Flyer	0.71 (0.43,1.16)	0.173
		Enlisted Groundcrew	0.89 (0.67,1.18)	0.431
9-9	Erythrocyte Sedimentation Rate	All	1.17 (0.84,1.63)	0.356
		Officer	0.86 (0.48,1.53)	0.602
		Enlisted Flyer	1.59 (0.75,3.38)	0.231
		Enlisted Groundcrew	1.29 (0.79,2.10)	0.305
10-3	Skin Neoplasms	All	1.32 (1.09,1.60)	0.005
		Officer	1.38 (1.03,1.85)	0.030
		Enlisted Flyer	1.66 (1.02,2.69)	0.040
		Enlisted Groundcrew	1.16 (0.86,1.56)	0.339
10-4	Malignant Skin Neoplasms	All	1.19 (0.93,1.54)	0.175
		Officer	1.29 (0.90,1.85)	0.161
		Enlisted Flyer	1.86 (0.99,3.51)	0.055
		Enlisted Groundcrew	0.86 (0.56,1.34)	0.509
10-5	Benign Skin Neoplasms	All	1.31 (1.07,1.61)	0.011
		Officer	1.41 (1.02,1.95)	0.035
		Enlisted Flyer	1.41 (0.82,2.43)	0.220
		Enlisted Groundcrew	1.20 (0.88,1.63)	0.257
10-6	Skin Neoplasms of Uncertain Behavior or Unspecified Nature	All	1.18 (0.42,3.36)	0.755
		Officer	--	--
		Enlisted Flyer	--	--
		Enlisted Groundcrew	2.57 (0.73,9.10)	0.144
10-7	Basal Cell Carcinoma	All	1.21 (0.92,1.59)	0.169
		Officer	1.34 (0.92,1.96)	0.129
		Enlisted Flyer	1.97 (1.01,3.85)	0.046
		Enlisted Groundcrew	0.80 (0.49,1.30)	0.363

Table G-17. Summary of Adjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value
10-8	Basal Cell Carcinoma (Ear, Face, Head, and Neck)	All	1.20 (0.89,1.62)	0.242
		Officer	1.29 (0.84,1.97)	0.244
		Enlisted Flyer	1.83 (0.90,3.72)	0.097
		Enlisted Groundcrew	0.84 (0.48,1.45)	0.527
10-9	Basal Cell Carcinoma (Trunk)	All	1.24 (0.79,1.94)	0.357
		Officer	1.47 (0.85,2.57)	0.170
		Enlisted Flyer	2.47 (0.59,10.26)	0.214
		Enlisted Groundcrew	0.52 (0.19,1.48)	0.222
10-10	Basal Cell Carcinoma (Upper Extremities)	All	0.76 (0.44,1.34)	0.340
		Officer	0.98 (0.51,1.89)	0.947
		Enlisted Flyer	0.56 (0.05,6.30)	0.635
		Enlisted Groundcrew	0.38 (0.11,1.37)	0.139
10-11	Basal Cell Carcinoma (Lower Extremities)	All	1.38 (0.39,4.85)	0.616
		Officer	1.83 (0.40,8.33)	0.436
		Enlisted Flyer	--	--
		Enlisted Groundcrew	0.78 (0.07,8.71)	0.839
10-12	Squamous Cell Carcinoma	All	1.46 (0.77,2.78)	0.250
		Officer	1.10 (0.49,2.49)	0.813
		Enlisted Flyer	1.86 (0.29,11.86)	0.514
		Enlisted Groundcrew	2.67 (0.73,9.76)	0.139
10-13	Nonmelanoma	All	1.18 (0.91,1.53)	0.219
		Officer	1.31 (0.91,1.90)	0.144
		Enlisted Flyer	2.00 (1.05,3.81)	0.035
		Enlisted Groundcrew	0.76 (0.48,1.22)	0.258
10-14	Melanoma	All	1.78 (0.83,3.79)	0.136
		Officer	1.92 (0.69,5.30)	0.211
		Enlisted Flyer	--	--
		Enlisted Groundcrew	2.01 (0.62,6.50)	0.246
10-15	Systemic Neoplasms (All Sites Combined)	All	0.88 (0.70,1.12)	0.307
		Officer	0.77 (0.56,1.07)	0.125
		Enlisted Flyer	0.98 (0.60,1.61)	0.937
		Enlisted Groundcrew	0.98 (0.70,1.36)	0.888
10-16	Malignant Systemic Neoplasms	All	1.12 (0.74,1.70)	0.592
		Officer	1.09 (0.63,1.88)	0.766
		Enlisted Flyer	1.91 (0.82,4.43)	0.132
		Enlisted Groundcrew	0.82 (0.41,1.67)	0.589
10-17	Benign Systemic Neoplasms	All	0.93 (0.73,1.19)	0.574
		Officer	0.78 (0.55,1.10)	0.155
		Enlisted Flyer	0.95 (0.56,1.59)	0.831
		Enlisted Groundcrew	1.11 (0.79,1.57)	0.548

Table G-17. Summary of Adjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value
10-18	Systemic Neoplasms of Uncertain Behavior or Unspecified Nature	All	0.71 (0.34,1.47)	0.355
		Officer	0.96 (0.40,2.31)	0.925
		Enlisted Flyer	0.45 (0.04,5.19)	0.523
		Enlisted Groundcrew	0.44 (0.13,1.50)	0.190
10-19	Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck)	All	0.98 (0.35,2.75)	0.974
		Officer	2.07 (0.53,8.16)	0.298
		Enlisted Flyer	0.38 (0.04,4.02)	0.424
		Enlisted Groundcrew	0.49 (0.08,2.87)	0.429
10-20	Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx)	All	0.63 (0.16,2.44)	0.501
		Officer	1.35 (0.17,10.61)	0.777
		Enlisted Flyer	0.52 (0.04,6.28)	0.603
		Enlisted Groundcrew	0.31 (0.03,3.40)	0.336
10-21	Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum)	All	--	--
		Officer	--	--
		Enlisted Flyer	--	--
		Enlisted Groundcrew	--	--
10-22	Malignant Systemic Neoplasms (Thyroid Gland)	All	1.46 (0.20,10.39)	0.708
		Officer	3.08 (0.28,34.40)	0.362
		Enlisted Flyer	--	--
		Enlisted Groundcrew	--	--
10-23	Malignant Systemic Neoplasms (Bronchus and Lung)	All	3.66 (0.78,17.13)	0.070
		Officer	3.51 (0.57,21.64)	0.176
		Enlisted Flyer	2.58 (0.21,31.26)	0.456
		Enlisted Groundcrew	--	--
10-24	Malignant Systemic Neoplasms (Liver)	All	1.57 (0.22,11.35)	0.655
		Officer	--	--
		Enlisted Flyer	--	--
		Enlisted Groundcrew	1.72 (0.11,27.93)	0.703
10-25	Malignant Systemic Neoplasms (Colon and Rectum)	All	1.50 (0.41,5.47)	0.536
		Officer	2.59 (0.37,17.95)	0.335
		Enlisted Flyer	1.57 (0.19,13.30)	0.678
		Enlisted Groundcrew	0.85 (0.13,5.78)	0.872
10-26	Malignant Systemic Neoplasms (Kidney and Bladder)	All	3.12 (0.88,11.04)	0.061
		Officer	1.86 (0.43,8.16)	0.409
		Enlisted Flyer	--	--
		Enlisted Groundcrew	4.20 (0.36,49.46)	0.254
10-27	Malignant Systemic Neoplasms (Prostate)	All	0.69 (0.38,1.25)	0.219
		Officer	0.58 (0.27,1.22)	0.151
		Enlisted Flyer	1.54 (0.41,5.75)	0.521
		Enlisted Groundcrew	0.59 (0.19,1.84)	0.360

Table G-17. Summary of Adjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value
10-28	Malignant Systemic Neoplasms (Testicles)	All	--	--
		Officer	--	--
		Enlisted Flyer	--	--
		Enlisted Groundcrew	--	--
10-29	Malignant Systemic Neoplasms (Connective and Other Soft Tissues)	All	0.79 (0.05,12.82)	0.870
		Officer	--	--
		Enlisted Flyer	--	--
		Enlisted Groundcrew	--	--
10-30	Hodgkin's Disease	All	0.29 (0.03,3.23)	0.291
		Officer	0.47 (0.04,5.86)	0.554
		Enlisted Flyer	--	--
		Enlisted Groundcrew	--	--
10-31	Non-Hodgkin's Lymphoma	All	0.18 (0.01,2.61)	0.186
		Officer	--	--
		Enlisted Flyer	--	--
		Enlisted Groundcrew	0.61 (0.02,15.18)	0.762
10-32	Other Malignant Systemic Neoplasms of Lymphoid and Histiocytic Tissue	All	0.70 (0.10,5.03)	0.724
		Officer	0.69 (0.05,9.34)	0.781
		Enlisted Flyer	--	--
		Enlisted Groundcrew	1.57 (0.08,31.01)	0.767
10-33	Malignant Skin and Systemic Neoplasms	All	1.06 (0.80,1.41)	0.668
		Officer	1.14 (0.79,1.65)	0.470
		Enlisted Flyer	1.63 (0.91,2.92)	0.103
		Enlisted Groundcrew	0.78 (0.51,1.19)	0.247
10-34	All Skin and Systemic Neoplasms	All	1.04 (0.83,1.30)	0.756
		Officer	1.06 (0.77,1.46)	0.725
		Enlisted Flyer	1.15 (0.72,1.84)	0.557
		Enlisted Groundcrew	0.98 (0.72,1.33)	0.881
10-36	PSA	All	1.02 (0.64,1.60)	0.947
		Officer	1.45 (0.80,2.63)	0.216
		Enlisted Flyer	0.78 (0.32,1.90)	0.578
		Enlisted Groundcrew	0.68 (0.33,1.41)	0.302
11-3	Inflammatory Diseases	All	13.50 (1.61,113.13)	0.002
		Officer	--	--
		Enlisted Flyer	--	--
		Enlisted Groundcrew	6.38 (0.64,63.30)	0.114
11-4	Hereditary and Degenerative Diseases	All	1.07 (0.78,1.46)	0.688
		Officer	1.13 (0.68,1.89)	0.635
		Enlisted Flyer	1.31 (0.66,2.62)	0.444
		Enlisted Groundcrew	0.92 (0.57,1.48)	0.737

Table G-17. Summary of Adjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value
11-5	Peripheral Disorders	All	1.12 (0.89,1.40)	0.341
		Officer	1.25 (0.88,1.78)	0.215
		Enlisted Flyer	0.91 (0.54,1.54)	0.733
		Enlisted Groundcrew	1.09 (0.77,1.54)	0.622
11-6	Other Neurological Disorders	All	1.25 (0.98,1.59)	0.078
		Officer	1.09 (0.65,1.84)	0.734
		Enlisted Flyer	1.33 (0.79,2.21)	0.283
		Enlisted Groundcrew	1.28 (0.92,1.78)	0.136
11-7	Smell	All	1.20 (0.60,2.36)	0.609
		Officer	0.53 (0.16,1.71)	0.286
		Enlisted Flyer	5.12 (0.56,46.70)	0.148
		Enlisted Groundcrew	1.57 (0.58,4.27)	0.376
11-8	Visual Fields	All	0.49 (0.09,2.64)	0.387
		Officer	--	--
		Enlisted Flyer	0.48 (0.04,5.78)	0.566
		Enlisted Groundcrew	0.70 (0.06,8.00)	0.778
11-9	Light Reaction	All	0.13 (0.02,0.98)	0.010
		Officer	--	--
		Enlisted Flyer	0.36 (0.04,3.38)	0.371
		Enlisted Groundcrew	--	--
11-10	Ocular Movement	All	1.17 (0.56,2.42)	0.675
		Officer	0.56 (0.11,2.90)	0.485
		Enlisted Flyer	1.76 (0.29,10.81)	0.543
		Enlisted Groundcrew	1.37 (0.54,3.45)	0.508
11-11	Facial Sensation	All	1.38 (0.19,9.87)	0.750
		Officer	1.45 (0.09,23.48)	0.792
		Enlisted Flyer	--	--
		Enlisted Groundcrew	--	--
11-12	Jaw Clench	All	--	--
		Officer	--	--
		Enlisted Flyer	--	--
		Enlisted Groundcrew	--	--
11-13	Smile	All	2.45 (0.71,8.50)	0.149
		Officer	0.71 (0.06,7.91)	0.777
		Enlisted Flyer	--	--
		Enlisted Groundcrew	3.62 (0.69,19.00)	0.128
11-14	Palpebral Fissure	All	0.71 (0.26,1.94)	0.502
		Officer	0.63 (0.12,3.31)	0.582
		Enlisted Flyer	0.87 (0.05,14.32)	0.921
		Enlisted Groundcrew	0.90 (0.25,3.27)	0.876

Table G-17. Summary of Adjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value
11-15	Balance	All	1.38 (0.47,4.03)	0.553
		Officer	3.37 (0.64,17.73)	0.151
		Enlisted Flyer	--	--
		Enlisted Groundcrew	0.73 (0.13,4.07)	0.719
11-16	Speech	All	0.60 (0.18,1.97)	0.388
		Officer	0.76 (0.07,8.59)	0.828
		Enlisted Flyer	--	--
		Enlisted Groundcrew	0.66 (0.16,2.63)	0.551
11-17	Tongue Position Relative to Midline	All	--	--
		Officer	--	--
		Enlisted Flyer	--	--
		Enlisted Groundcrew	--	--
11-18	Palate and Uvula Movement	All	--	--
		Officer	--	--
		Enlisted Flyer	--	--
		Enlisted Groundcrew	--	--
11-19	Cranial Nerve Index	All	1.01 (0.69,1.48)	0.940
		Officer	0.88 (0.46,1.68)	0.694
		Enlisted Flyer	1.23 (0.49,3.08)	0.656
		Enlisted Groundcrew	1.05 (0.61,1.80)	0.856
11-20	Neck Range of Motion	All	1.35 (1.06,1.72)	0.015
		Officer	1.31 (0.90,1.89)	0.153
		Enlisted Flyer	1.97 (1.13,3.42)	0.016
		Enlisted Groundcrew	1.16 (0.78,1.71)	0.466
11-21	Pinprick	All	1.19 (0.81,1.76)	0.368
		Officer	1.28 (0.67,2.43)	0.451
		Enlisted Flyer	1.81 (0.84,3.89)	0.131
		Enlisted Groundcrew	0.85 (0.45,1.60)	0.618
11-22	Light Touch	All	1.13 (0.71,1.81)	0.597
		Officer	1.67 (0.77,3.61)	0.193
		Enlisted Flyer	1.40 (0.56,3.50)	0.470
		Enlisted Groundcrew	0.67 (0.31,1.47)	0.321
11-23	Muscle Status	All	1.50 (0.93,2.40)	0.094
		Officer	0.98 (0.47,2.05)	0.960
		Enlisted Flyer	1.72 (0.63,4.70)	0.289
		Enlisted Groundcrew	2.24 (1.01,4.93)	0.046
11-24	Patellar Reflex	All	0.97 (0.56,1.67)	0.910
		Officer	1.05 (0.48,2.29)	0.901
		Enlisted Flyer	0.16 (0.02,1.32)	0.089
		Enlisted Groundcrew	1.43 (0.61,3.34)	0.408

Table G-17. Summary of Adjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value
11-25	Achilles Reflex	All	1.07 (0.84,1.37)	0.594
		Officer	1.17 (0.80,1.70)	0.413
		Enlisted Flyer	0.91 (0.51,1.60)	0.737
		Enlisted Groundcrew	1.05 (0.71,1.55)	0.815
11-26	Biceps Reflex	All	1.31 (0.57,3.05)	0.527
		Officer	1.13 (0.33,3.80)	0.848
		Enlisted Flyer	1.34 (0.18,9.89)	0.776
		Enlisted Groundcrew	1.61 (0.39,6.58)	0.509
11-27	Babinski Reflex	All	0.81 (0.31,2.10)	0.666
		Officer	2.16 (0.35,13.17)	0.403
		Enlisted Flyer	0.36 (0.04,3.59)	0.385
		Enlisted Groundcrew	0.64 (0.16,2.51)	0.526
11-29	Polyneuropathy Prevalence Index	All	0.99 (0.76,1.28)	0.923
		Officer	1.02 (0.68,1.51)	0.941
		Enlisted Flyer	0.86 (0.48,1.52)	0.601
		Enlisted Groundcrew	1.03 (0.67,1.59)	0.877
11-30	Multiple Polyneuropathy Index	All	1.51 (0.94,2.45)	0.092
		Officer	1.44 (0.69,2.98)	0.330
		Enlisted Flyer	1.77 (0.69,4.56)	0.234
		Enlisted Groundcrew	1.43 (0.60,3.39)	0.421
11-31	Confirmed Polyneuropathy Indicator	All	2.35 (0.88,6.22)	0.082
		Officer	0.51 (0.10,2.59)	0.414
		Enlisted Flyer	--	--
		Enlisted Groundcrew	8.59 (0.97,76.27)	0.054
11-32	Tremor	All	0.90 (0.64,1.28)	0.564
		Officer	1.06 (0.59,1.89)	0.850
		Enlisted Flyer	1.14 (0.53,2.44)	0.734
		Enlisted Groundcrew	0.72 (0.42,1.21)	0.212
11-33	Coordination	All	0.86 (0.48,1.56)	0.622
		Officer	1.65 (0.64,4.26)	0.302
		Enlisted Flyer	0.28 (0.03,2.58)	0.263
		Enlisted Groundcrew	0.64 (0.27,1.50)	0.305
11-34	Romberg Sign	All	1.38 (0.47,4.03)	0.553
		Officer	3.37 (0.64,17.73)	0.151
		Enlisted Flyer	--	--
		Enlisted Groundcrew	0.73 (0.13,4.07)	0.719
11-35	Gait	All	1.26 (0.83,1.89)	0.275
		Officer	1.01 (0.54,1.89)	0.972
		Enlisted Flyer	1.05 (0.43,2.59)	0.911
		Enlisted Groundcrew	1.79 (0.91,3.49)	0.090

Table G-17. Summary of Adjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value
11-36	CNS Index	All	0.99 (0.75,1.31)	0.957
		Officer	1.01 (0.64,1.58)	0.975
		Enlisted Flyer	0.92 (0.50,1.70)	0.799
		Enlisted Groundcrew	1.01 (0.67,1.54)	0.950
12-3	Psychoses	All	1.03 (0.65,1.63)	0.905
		Officer	1.12 (0.47,2.71)	0.796
		Enlisted Flyer	1.85 (0.68,5.04)	0.230
		Enlisted Groundcrew	0.76 (0.40,1.47)	0.423
12-4	Alcohol Dependence	All	1.04 (0.74,1.48)	0.816
		Officer	0.82 (0.43,1.58)	0.557
		Enlisted Flyer	0.94 (0.43,2.04)	0.871
		Enlisted Groundcrew	1.25 (0.76,2.03)	0.377
12-5	Drug Dependence	All	0.58 (0.09,3.74)	0.553
		Officer	--	--
		Enlisted Flyer	--	--
		Enlisted Groundcrew	0.78 (0.11,5.56)	0.802
12-6	Anxiety	All	1.00 (0.82,1.23)	0.979
		Officer	0.93 (0.64,1.35)	0.709
		Enlisted Flyer	1.01 (0.63,1.63)	0.953
		Enlisted Groundcrew	1.04 (0.79,1.38)	0.776
12-7	Other Neuroses	All	1.08 (0.90,1.29)	0.434
		Officer	0.80 (0.60,1.07)	0.127
		Enlisted Flyer	1.04 (0.66,1.65)	0.857
		Enlisted Groundcrew	1.44 (1.09,1.91)	0.011
12-8	SCL-90-R Anxiety	All	0.85 (0.63,1.14)	0.267
		Officer	0.75 (0.39,1.46)	0.400
		Enlisted Flyer	0.53 (0.27,1.06)	0.073
		Enlisted Groundcrew	1.02 (0.70,1.50)	0.904
12-9	SCL-90-R Depression	All	0.79 (0.61,1.03)	0.077
		Officer	0.89 (0.54,1.46)	0.642
		Enlisted Flyer	0.45 (0.24,0.84)	0.013
		Enlisted Groundcrew	0.90 (0.64,1.28)	0.562
12-10	SCL-90-R Hostility	All	0.81 (0.58,1.13)	0.217
		Officer	0.71 (0.34,1.49)	0.367
		Enlisted Flyer	0.66 (0.30,1.45)	0.301
		Enlisted Groundcrew	0.90 (0.59,1.39)	0.642
12-11	SCL-90-R Interpersonal Sensitivity	All	0.79 (0.61,1.02)	0.070
		Officer	0.93 (0.55,1.56)	0.772
		Enlisted Flyer	0.52 (0.28,0.93)	0.029
		Enlisted Groundcrew	0.86 (0.61,1.20)	0.366

Table G-17. Summary of Adjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value
12-12	SCL-90-R Obsessive-Compulsive Behavior	All	0.83 (0.65,1.07)	0.157
		Officer	0.95 (0.58,1.54)	0.824
		Enlisted Flyer	0.77 (0.44,1.35)	0.365
		Enlisted Groundcrew	0.81 (0.57,1.14)	0.225
12-13	SCL-90-R Paranoid Ideation	All	0.98 (0.68,1.40)	0.898
		Officer	0.84 (0.35,2.03)	0.698
		Enlisted Flyer	0.56 (0.23,1.37)	0.206
		Enlisted Groundcrew	1.17 (0.76,1.81)	0.479
12-14	SCL-90-R Phobic Anxiety	All	0.92 (0.68,1.24)	0.570
		Officer	0.53 (0.25,1.11)	0.090
		Enlisted Flyer	0.59 (0.29,1.18)	0.136
		Enlisted Groundcrew	1.24 (0.85,1.81)	0.270
12-15	SCL-90-R Psychoticism	All	0.81 (0.62,1.06)	0.116
		Officer	0.68 (0.39,1.17)	0.162
		Enlisted Flyer	0.67 (0.36,1.27)	0.223
		Enlisted Groundcrew	0.92 (0.65,1.31)	0.651
12-16	SCL-90-R Somatization	All	1.02 (0.80,1.31)	0.847
		Officer	1.02 (0.60,1.74)	0.948
		Enlisted Flyer	0.67 (0.40,1.13)	0.133
		Enlisted Groundcrew	1.22 (0.88,1.70)	0.232
12-17	SCL-90-R Global Severity Index (GSI)	All	0.87 (0.67,1.13)	0.285
		Officer	0.93 (0.54,1.61)	0.805
		Enlisted Flyer	0.57 (0.32,1.04)	0.066
		Enlisted Groundcrew	0.97 (0.70,1.36)	0.876
12-18	SCL-90-R Positive Symptom Total (PST)	All	0.80 (0.62,1.03)	0.083
		Officer	0.80 (0.48,1.33)	0.382
		Enlisted Flyer	0.67 (0.38,1.18)	0.168
		Enlisted Groundcrew	0.86 (0.61,1.20)	0.365
12-19	SCL-90-R Positive Symptom Distress Index (PSDI)	All	1.20 (0.86,1.69)	0.283
		Officer	1.29 (0.62,2.68)	0.495
		Enlisted Flyer	0.78 (0.36,1.66)	0.513
		Enlisted Groundcrew	1.37 (0.88,2.12)	0.165
13-3	Uncharacterized Hepatitis	All	1.18 (0.62,2.26)	0.617
		Officer	1.05 (0.33,3.35)	0.935
		Enlisted Flyer	1.62 (0.35,7.40)	0.533
		Enlisted Groundcrew	1.13 (0.45,2.85)	0.795
13-4	Jaundice	All	0.49 (0.25,0.96)	0.028
		Officer	0.46 (0.18,1.17)	0.103
		Enlisted Flyer	3.47 (0.36,33.8)	0.284
		Enlisted Groundcrew	0.29 (0.08,1.03)	0.055

Table G-17. Summary of Adjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value
13-5	Chronic Liver Disease and Cirrhosis (Alcohol-related)	All	0.93 (0.60,1.45)	0.762
		Officer	1.50 (0.71,3.19)	0.290
		Enlisted Flyer	0.70 (0.26,1.88)	0.474
		Enlisted Groundcrew	0.75 (0.39,1.45)	0.390
13-6	Chronic Liver Disease and Cirrhosis (Non-alcohol-related)	All	1.43 (0.68,3.03)	0.348
		Officer	2.47 (0.58,10.52)	0.219
		Enlisted Flyer	0.77 (0.13,4.71)	0.777
		Enlisted Groundcrew	1.32 (0.47,3.69)	0.598
13-7	Liver Abscess and Sequelae of Chronic Liver Disease	All	1.45 (0.09,23.24)	0.795
		Officer	--	--
		Enlisted Flyer	--	--
		Enlisted Groundcrew	--	--
13-8	Enlarged Liver (Hepatomegaly)	All	0.73 (0.38,1.41)	0.339
		Officer	0.78 (0.26,2.36)	0.662
		Enlisted Flyer	2.53 (0.62,10.38)	0.198
		Enlisted Groundcrew	0.29 (0.08,1.03)	0.057
13-9	Other Liver Disorders	All	1.19 (0.97,1.45)	0.090
		Officer	1.15 (0.83,1.57)	0.400
		Enlisted Flyer	0.98 (0.60,1.61)	0.933
		Enlisted Groundcrew	1.31 (0.98,1.75)	0.073
13-10	Current Hepatomegaly	All	2.13 (0.80,5.67)	0.127
		Officer	3.17 (0.57,17.56)	0.187
		Enlisted Flyer	--	--
		Enlisted Groundcrew	1.18 (0.31,4.51)	0.805
13-12	AST	All	1.14 (0.81,1.61)	0.448
		Officer	1.09 (0.63,1.89)	0.763
		Enlisted Flyer	0.84 (0.36,1.92)	0.671
		Enlisted Groundcrew	1.35 (0.81,2.28)	0.252
13-14	ALT	All	1.12 (0.80,1.57)	0.495
		Officer	1.58 (0.86,2.89)	0.138
		Enlisted Flyer	0.97 (0.46,2.01)	0.927
		Enlisted Groundcrew	0.97 (0.60,1.57)	0.889
13-16	GGT	All	1.08 (0.80,1.45)	0.604
		Officer	1.24 (0.75,2.06)	0.399
		Enlisted Flyer	1.39 (0.73,2.65)	0.310
		Enlisted Groundcrew	0.86 (0.55,1.35)	0.512
13-18	Alkaline Phosphatase	All	1.34 (0.74,2.42)	0.332
		Officer	0.45 (0.14,1.41)	0.172
		Enlisted Flyer	2.03 (0.56,7.40)	0.284
		Enlisted Groundcrew	2.46 (0.99,6.13)	0.053

Table G-17. Summary of Adjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value
13-20	Total Bilirubin	All	0.86 (0.58,1.25)	0.420
		Officer	0.90 (0.52,1.57)	0.723
		Enlisted Flyer	1.15 (0.43,3.08)	0.779
		Enlisted Groundcrew	0.71 (0.38,1.33)	0.286
13-21	Direct Bilirubin	All	0.32 (0.04,2.82)	0.254
		Officer	0.50 (0.05,4.90)	0.551
		Enlisted Flyer	--	--
		Enlisted Groundcrew	--	--
13-23	Lactic Dehydrogenase	All	0.90 (0.67,1.21)	0.479
		Officer	0.86 (0.54,1.37)	0.530
		Enlisted Flyer	1.03 (0.47,2.24)	0.945
		Enlisted Groundcrew	0.90 (0.58,1.39)	0.625
13-25	Cholesterol	All	1.04 (0.82,1.34)	0.726
		Officer	0.80 (0.53,1.23)	0.312
		Enlisted Flyer	1.00 (0.54,1.83)	0.993
		Enlisted Groundcrew	1.28 (0.90,1.82)	0.167
13-27	HDL Cholesterol	All	1.13 (0.81,1.57)	0.473
		Officer	1.15 (0.62,2.15)	0.650
		Enlisted Flyer	0.98 (0.47,2.04)	0.957
		Enlisted Groundcrew	1.18 (0.74,1.87)	0.483
13-29	Cholesterol-HDL Ratio	All	1.01 (0.85,1.22)	0.878
		Officer	1.09 (0.81,1.47)	0.563
		Enlisted Flyer	0.67 (0.43,1.04)	0.075
		Enlisted Groundcrew	1.11 (0.85,1.45)	0.436
13-31	Triglycerides	All	1.12 (0.90,1.39)	0.318
		Officer	1.10 (0.76,1.58)	0.628
		Enlisted Flyer	0.66 (0.39,1.12)	0.123
		Enlisted Groundcrew	1.37 (1.00,1.88)	0.047
13-33	Creatine Phosphokinase	All	0.87 (0.63,1.20)	0.390
		Officer	0.84 (0.50,1.41)	0.519
		Enlisted Flyer	0.55 (0.21,1.41)	0.210
		Enlisted Groundcrew	1.00 (0.63,1.58)	0.998
13-35	Serum Amylase	All	0.91 (0.54,1.54)	0.733
		Officer	0.43 (0.18,1.03)	0.058
		Enlisted Flyer	1.66 (0.36,7.69)	0.514
		Enlisted Groundcrew	1.60 (0.73,3.50)	0.240
13-36	Antibodies for Hepatitis A	All	0.93 (0.76,1.12)	0.434
		Officer	0.95 (0.68,1.31)	0.739
		Enlisted Flyer	1.07 (0.69,1.68)	0.754
		Enlisted Groundcrew	0.85 (0.64,1.14)	0.285

Table G-17. Summary of Adjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value
13-37	Prior Hepatitis B	All	0.59 (0.44,0.80)	<0.001
		Officer	0.47 (0.25,0.91)	0.024
		Enlisted Flyer	0.58 (0.31,1.07)	0.079
		Enlisted Groundcrew	0.66 (0.44,0.97)	0.035
13-38	Current Hepatitis B	All	0.56 (0.05,6.93)	0.646
		Officer	--	--
		Enlisted Flyer	--	--
		Enlisted Groundcrew	0.68 (0.06,8.27)	0.762
13-39	Antibodies for Hepatitis C	All	0.63 (0.27,1.47)	0.274
		Officer	0.36 (0.04,3.27)	0.367
		Enlisted Flyer	0.61 (0.05,6.87)	0.690
		Enlisted Groundcrew	0.73 (0.27,1.98)	0.532
13-40	Stool Hemoccult	All	0.78 (0.49,1.25)	0.301
		Officer	0.90 (0.45,1.80)	0.774
		Enlisted Flyer	0.34 (0.07,1.70)	0.191
		Enlisted Groundcrew	0.82 (0.41,1.64)	0.574
13-42	Prealbumin	All	1.87 (0.82,4.26)	0.136
		Officer	1.03 (0.32,3.29)	0.962
		Enlisted Flyer	1.64 (0.09,28.94)	0.736
		Enlisted Groundcrew	4.27 (1.05,17.39)	0.043
13-44	Albumin	All	0.45 (0.12,1.65)	0.200
		Officer	1.08 (0.24,4.91)	0.918
		Enlisted Flyer	--	--
		Enlisted Groundcrew	--	--
13-46	α-1-Acid Glycoprotein	All	1.39 (0.88,2.21)	0.163
		Officer	0.73 (0.31,1.76)	0.487
		Enlisted Flyer	1.78 (0.64,4.95)	0.270
		Enlisted Groundcrew	1.86 (0.96,3.60)	0.066
13-50	α-2-Macroglobulin	All	0.70 (0.42,1.16)	0.157
		Officer	0.59 (0.25,1.40)	0.234
		Enlisted Flyer	0.46 (0.15,1.39)	0.169
		Enlisted Groundcrew	1.01 (0.46,2.19)	0.988
13-52	Apolipoprotein B	All	0.85 (0.71,1.02)	0.073
		Officer	0.80 (0.61,1.06)	0.115
		Enlisted Flyer	0.53 (0.34,0.82)	0.005
		Enlisted Groundcrew	1.07 (0.82,1.40)	0.603
13-54	C3 Complement	All	0.79 (0.42,1.50)	0.474
		Officer	0.62 (0.23,1.63)	0.333
		Enlisted Flyer	0.27 (0.03,2.33)	0.233
		Enlisted Groundcrew	1.41 (0.54,3.71)	0.487

Table G-17. Summary of Adjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value
13-56	C4 Complement	All	1.46 (0.20,10.59)	0.707
		Officer	2.85 (0.26,31.68)	0.394
		Enlisted Flyer	--	--
		Enlisted Groundcrew	--	--
13-58	Haptoglobin	All	1.26 (1.04,1.52)	0.020
		Officer	1.18 (0.85,1.64)	0.316
		Enlisted Flyer	1.27 (0.81,2.01)	0.295
		Enlisted Groundcrew	1.31 (0.99,1.73)	0.061
13-60	Transferrin	All	0.71 (0.52,0.97)	0.027
		Officer	0.63 (0.38,1.04)	0.070
		Enlisted Flyer	0.83 (0.41,1.68)	0.601
		Enlisted Groundcrew	0.74 (0.47,1.18)	0.208
14-3	Essential Hypertension	All	0.96 (0.79,1.17)	0.708
		Officer	0.85 (0.63,1.16)	0.317
		Enlisted Flyer	1.27 (0.79,2.04)	0.316
		Enlisted Groundcrew	0.96 (0.72,1.29)	0.811
14-4	Heart Disease (Excluding Essential Hypertension)	All	1.26 (1.04,1.53)	0.018
		Officer	1.21 (0.88,1.66)	0.238
		Enlisted Flyer	2.10 (1.28,3.45)	0.004
		Enlisted Groundcrew	1.10 (0.83,1.46)	0.496
14-5	Myocardial Infarction	All	1.02 (0.73,1.42)	0.915
		Officer	0.86 (0.50,1.46)	0.567
		Enlisted Flyer	1.57 (0.72,3.43)	0.255
		Enlisted Groundcrew	0.99 (0.59,1.67)	0.975
14-6	Stroke or Transient Ischemia Attack	All	1.21 (0.51,2.85)	0.666
		Officer	1.18 (0.31,4.51)	0.806
		Enlisted Flyer	--	--
		Enlisted Groundcrew	1.80 (0.53,6.06)	0.345
14-8	Systolic Blood Pressure	All	0.99 (0.79,1.24)	0.899
		Officer	0.95 (0.67,1.35)	0.784
		Enlisted Flyer	1.13 (0.66,1.93)	0.661
		Enlisted Groundcrew	0.96 (0.67,1.38)	0.832
14-10	Diastolic Blood Pressure	All	1.02 (0.67,1.56)	0.916
		Officer	1.21 (0.62,2.35)	0.576
		Enlisted Flyer	1.18 (0.41,3.37)	0.760
		Enlisted Groundcrew	0.84 (0.44,1.59)	0.584
14-11	Heart Sounds	All	0.71 (0.45,1.13)	0.139
		Officer	0.60 (0.28,1.29)	0.190
		Enlisted Flyer	0.65 (0.23,1.84)	0.419
		Enlisted Groundcrew	0.86 (0.42,1.74)	0.675

Table G-17. Summary of Adjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value
14-12	Overall Electrocardiograph	All	0.96 (0.78,1.18)	0.688
		Officer	1.07 (0.79,1.47)	0.655
		Enlisted Flyer	1.24 (0.76,2.00)	0.389
		Enlisted Groundcrew	0.76 (0.55,1.05)	0.095
14-13	Right Bundle Branch Block	All	0.88 (0.49,1.56)	0.650
		Officer	0.89 (0.36,2.22)	0.807
		Enlisted Flyer	1.47 (0.49,4.44)	0.493
		Enlisted Groundcrew	0.55 (0.19,1.59)	0.271
14-14	Left Bundle Branch Block	All	0.47 (0.15,1.50)	0.182
		Officer	0.21 (0.02,1.76)	0.150
		Enlisted Flyer	--	--
		Enlisted Groundcrew	0.56 (0.11,2.83)	0.479
14-15	Non-Specific ST- and T-Wave Changes	All	1.00 (0.79,1.27)	0.984
		Officer	1.03 (0.71,1.48)	0.882
		Enlisted Flyer	1.22 (0.69,2.14)	0.495
		Enlisted Groundcrew	0.88 (0.60,1.29)	0.517
14-16	Bradycardia	All	0.69 (0.41,1.16)	0.151
		Officer	0.74 (0.38,1.42)	0.360
		Enlisted Flyer	1.14 (0.32,4.09)	0.846
		Enlisted Groundcrew	0.36 (0.10,1.30)	0.120
14-17	Tachycardia	All	2.94 (0.69,12.51)	0.129
		Officer	--	--
		Enlisted Flyer	--	--
		Enlisted Groundcrew	1.54 (0.19,12.63)	0.685
14-18	Arrhythmia	All	1.02 (0.69,1.52)	0.913
		Officer	1.39 (0.75,2.55)	0.296
		Enlisted Flyer	1.26 (0.54,2.97)	0.591
		Enlisted Groundcrew	0.62 (0.31,1.25)	0.180
14-19	Evidence of Prior Myocardial Infarction	All	0.90 (0.56,1.43)	0.649
		Officer	0.88 (0.43,1.78)	0.718
		Enlisted Flyer	1.02 (0.35,2.96)	0.972
		Enlisted Groundcrew	0.86 (0.40,1.85)	0.709
14-20	ECG: Other Diagnoses	All	4.67 (0.47,46.79)	0.153
		Officer	--	--
		Enlisted Flyer	--	--
		Enlisted Groundcrew	3.29 (0.28,38.94)	0.346
14-21	Funduscopic Examination	All	0.92 (0.69,1.22)	0.562
		Officer	1.27 (0.79,2.02)	0.321
		Enlisted Flyer	1.06 (0.59,1.91)	0.852
		Enlisted Groundcrew	0.62 (0.39,0.99)	0.047

Table G-17. Summary of Adjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value
14-22	Carotid Bruits	All	0.94 (0.53,1.65)	0.823
		Officer	0.72 (0.26,1.99)	0.524
		Enlisted Flyer	1.94 (0.58,6.46)	0.283
		Enlisted Groundcrew	0.78 (0.33,1.86)	0.578
14-23	Radial Pulses	All	2.85 (0.67,12.16)	0.143
		Officer	1.24 (0.16,9.95)	0.837
		Enlisted Flyer	--	--
		Enlisted Groundcrew	5.69 (0.54,60.05)	0.148
14-24	Femoral Pulses	All	1.66 (0.79,3.49)	0.178
		Officer	1.51 (0.52,4.38)	0.448
		Enlisted Flyer	1.48 (0.27,8.02)	0.652
		Enlisted Groundcrew	2.08 (0.55,7.87)	0.282
14-25	Popliteal Pulses	All	1.04 (0.56,1.90)	0.911
		Officer	0.95 (0.35,2.52)	0.911
		Enlisted Flyer	0.99 (0.21,4.82)	0.995
		Enlisted Groundcrew	1.13 (0.46,2.79)	0.784
14-26	Dorsalis Pedis Pulses	All	0.97 (0.69,1.37)	0.857
		Officer	1.27 (0.73,2.22)	0.398
		Enlisted Flyer	1.33 (0.62,2.86)	0.463
		Enlisted Groundcrew	0.64 (0.37,1.12)	0.117
14-27	Posterior Tibial Pulses	All	1.25 (0.84,1.86)	0.280
		Officer	1.40 (0.73,2.68)	0.307
		Enlisted Flyer	1.17 (0.49,2.78)	0.724
		Enlisted Groundcrew	1.16 (0.62,2.16)	0.649
14-28	Leg Pulses	All	1.03 (0.76,1.40)	0.850
		Officer	1.30 (0.79,2.16)	0.306
		Enlisted Flyer	1.46 (0.74,2.88)	0.270
		Enlisted Groundcrew	0.71 (0.44,1.14)	0.158
14-29	Peripheral Pulses	All	1.05 (0.77,1.42)	0.761
		Officer	1.27 (0.77,2.09)	0.353
		Enlisted Flyer	1.48 (0.75,2.92)	0.260
		Enlisted Groundcrew	0.75 (0.47,1.21)	0.242
14-30	ICVI Index	All	0.99 (0.61,1.60)	0.958
		Officer	1.25 (0.57,2.70)	0.577
		Enlisted Flyer	0.50 (0.17,1.51)	0.218
		Enlisted Groundcrew	1.12 (0.53,2.39)	0.764
15-14	Prothrombin Time	All	1.13 (0.49,2.60)	0.781
		Officer	1.29 (0.43,3.91)	0.650
		Enlisted Flyer	--	--
		Enlisted Groundcrew	1.15 (0.30,4.35)	0.838

Table G-17. Summary of Adjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value
15-15	RBC Morphology	All	1.16 (0.82,1.64)	0.400
		Officer	1.03 (0.57,1.87)	0.923
		Enlisted Flyer	1.09 (0.52,2.30)	0.814
		Enlisted Groundcrew	1.31 (0.78,2.22)	0.307
15-18	Absolute Neutrophils (bands) (Zero vs. Nonzero)	All	0.99 (0.79,1.25)	0.956
		Officer	0.74 (0.51,1.09)	0.134
		Enlisted Flyer	1.88 (1.08,3.27)	0.026
		Enlisted Groundcrew	0.98 (0.69,1.39)	0.918
15-22	Absolute Eosinophils (Zero vs. Nonzero)	All	1.01 (0.77,1.31)	0.970
		Officer	1.18 (0.74,1.87)	0.489
		Enlisted Flyer	0.95 (0.49,1.87)	0.893
		Enlisted Groundcrew	0.92 (0.64,1.34)	0.674
15-24	Absolute Basophils (Zero vs. Nonzero)	All	1.16 (0.97,1.38)	0.106
		Officer	1.16 (0.88,1.53)	0.303
		Enlisted Flyer	0.87 (0.57,1.34)	0.529
		Enlisted Groundcrew	1.28 (0.98,1.68)	0.065
16-3	Past Thyroid Disease	All	0.89 (0.64,1.22)	0.459
		Officer	0.91 (0.56,1.48)	0.701
		Enlisted Flyer	1.37 (0.64,2.94)	0.419
		Enlisted Groundcrew	0.70 (0.41,1.19)	0.189
16-4	Composite Diabetes Indicator	All	1.04 (0.81,1.33)	0.755
		Officer	1.08 (0.72,1.63)	0.711
		Enlisted Flyer	0.82 (0.45,1.47)	0.498
		Enlisted Groundcrew	1.11 (0.77,1.61)	0.572
16-7	Thyroid Gland	All	0.54 (0.21,1.39)	0.183
		Officer	0.53 (0.17,1.67)	0.276
		Enlisted Flyer	1.23 (0.08,19.88)	0.883
		Enlisted Groundcrew	0.38 (0.04,3.39)	0.384
16-8	Testicular Examination	All	1.20 (0.77,1.87)	0.427
		Officer	0.84 (0.44,1.62)	0.611
		Enlisted Flyer	1.31 (0.48,3.55)	0.595
		Enlisted Groundcrew	1.96 (0.88,4.39)	0.101
16-12	Thyroxine	All	1.04 (0.61,1.80)	0.875
		Officer	1.21 (0.57,2.55)	0.622
		Enlisted Flyer	1.24 (0.25,6.24)	0.796
		Enlisted Groundcrew	0.80 (0.32,2.02)	0.636
16-13	Anti-Thyroid Antibodies	All	1.01 (0.32,3.21)	0.981
		Officer	0.73 (0.13,4.02)	0.717
		Enlisted Flyer	2.62 (0.24,29.23)	0.434
		Enlisted Groundcrew	0.73 (0.07,8.06)	0.796

Table G-17. Summary of Adjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value
16-15	Fasting Glucose	All	1.07 (0.84,1.37)	0.562
		Officer	1.11 (0.75,1.64)	0.611
		Enlisted Flyer	0.90 (0.50,1.60)	0.712
		Enlisted Groundcrew	1.12 (0.78,1.61)	0.526
16-17	2-Hour Postprandial Glucose	All	0.98 (0.75,1.30)	0.912
		Officer	1.42 (0.92,2.20)	0.110
		Enlisted Flyer	0.81 (0.43,1.54)	0.526
		Enlisted Groundcrew	0.75 (0.48,1.16)	0.191
16-18	Fasting Urinary Glucose	All	0.98 (0.63,1.52)	0.924
		Officer	1.40 (0.61,3.22)	0.432
		Enlisted Flyer	1.13 (0.41,3.11)	0.816
		Enlisted Groundcrew	0.77 (0.42,1.43)	0.412
16-19	2-Hour Postprandial Urinary Glucose	All	1.22 (0.97,1.53)	0.094
		Officer	1.47 (1.01,2.14)	0.044
		Enlisted Flyer	0.73 (0.42,1.28)	0.276
		Enlisted Groundcrew	1.26 (0.90,1.76)	0.180
16-23	α-1-C Hemoglobin	All	1.14 (0.85,1.53)	0.373
		Officer	1.13 (0.67,1.90)	0.652
		Enlisted Flyer	0.65 (0.33,1.28)	0.210
		Enlisted Groundcrew	1.43 (0.95,2.16)	0.087
16-25	Total Testosterone	All	1.16 (0.83,1.63)	0.378
		Officer	1.22 (0.71,2.07)	0.475
		Enlisted Flyer	1.21 (0.50,2.96)	0.673
		Enlisted Groundcrew	1.11 (0.67,1.83)	0.688
16-27	Free Testosterone	All	1.09 (0.54,2.19)	0.812
		Officer	1.06 (0.39,2.90)	0.911
		Enlisted Flyer	6.41 (0.74,55.13)	0.091
		Enlisted Groundcrew	0.37 (0.08,1.76)	0.210
16-29	Estradiol	All	0.95 (0.78,1.16)	0.619
		Officer	0.78 (0.56,1.07)	0.120
		Enlisted Flyer	0.89 (0.56,1.42)	0.616
		Enlisted Groundcrew	1.16 (0.87,1.55)	0.312
16-31	LH	All	1.02 (0.70,1.50)	0.907
		Officer	1.24 (0.70,2.20)	0.458
		Enlisted Flyer	0.86 (0.29,2.55)	0.782
		Enlisted Groundcrew	0.88 (0.49,1.59)	0.674
16-33	FSH	All	1.04 (0.75,1.45)	0.794
		Officer	1.18 (0.74,1.85)	0.488
		Enlisted Flyer	1.49 (0.70,3.17)	0.297
		Enlisted Groundcrew	0.68 (0.37,1.26)	0.221

Table G-17. Summary of Adjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value
17-14	ANA Test	All	1.01 (0.84,1.20)	0.946
		Officer	0.95 (0.72,1.27)	0.736
		Enlisted Flyer	1.07 (0.68,1.67)	0.778
		Enlisted Groundcrew	1.04 (0.79,1.36)	0.801
17-15	Thyroid Microsomal Antibody	All	1.02 (0.59,1.75)	0.947
		Officer	1.14 (0.51,2.55)	0.750
		Enlisted Flyer	0.75 (0.17,3.19)	0.692
		Enlisted Groundcrew	1.00 (0.43,2.35)	0.994
17-16	MSK Smooth Muscle Antibody	All	0.99 (0.75,1.31)	0.953
		Officer	1.30 (0.84,2.03)	0.239
		Enlisted Flyer	0.48 (0.24,0.99)	0.045
		Enlisted Groundcrew	1.02 (0.68,1.53)	0.934
17-17	MSK Mitochondrial Antibody	All	2.79 (0.51,15.31)	0.222
		Officer	6.58 (0.70,61.53)	0.098
		Enlisted Flyer	--	--
		Enlisted Groundcrew	--	--
17-18	MSK Parietal Antibody	All	1.00 (0.64,1.56)	0.996
		Officer	1.36 (0.65,2.87)	0.416
		Enlisted Flyer	0.58 (0.19,1.74)	0.331
		Enlisted Groundcrew	0.97 (0.51,1.85)	0.920
17-19	Rheumatoid Factor	All	0.91 (0.69,1.22)	0.540
		Officer	1.09 (0.71,1.68)	0.692
		Enlisted Flyer	0.98 (0.51,1.91)	0.956
		Enlisted Groundcrew	0.71 (0.44,1.15)	0.167
18-3	Asthma	All	1.36 (0.87,2.10)	0.175
		Officer	1.48 (0.74,2.94)	0.266
		Enlisted Flyer	0.45 (0.12,1.74)	0.247
		Enlisted Groundcrew	1.69 (0.89,3.21)	0.111
18-4	Bronchitis	All	1.15 (0.92,1.43)	0.213
		Officer	1.02 (0.70,1.47)	0.936
		Enlisted Flyer	1.61 (0.95,2.71)	0.075
		Enlisted Groundcrew	1.11 (0.81,1.54)	0.514
18-5	Pneumonia	All	0.87 (0.66,1.16)	0.354
		Officer	0.74 (0.47,1.16)	0.185
		Enlisted Flyer	1.75 (0.85,3.61)	0.126
		Enlisted Groundcrew	0.79 (0.50,1.24)	0.304

Table G-17. Summary of Adjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value
18-6	Thorax and Lung Abnormalities	All	0.97 (0.71,1.31)	0.821
		Officer	1.57 (0.90,2.71)	0.110
		Enlisted Flyer	0.99 (0.53,1.85)	0.978
		Enlisted Groundcrew	0.69 (0.44,1.09)	0.115
18-7	X-ray Interpretation	All	1.23 (0.92,1.64)	0.158
		Officer	1.39 (0.87,2.20)	0.167
		Enlisted Flyer	1.16 (0.56,2.39)	0.685
		Enlisted Groundcrew	1.14 (0.75,1.73)	0.554

--: Relative risk, confidence interval, and p-value are not presented because of the sparse number of participants with abnormalities.

Table G-18. Summary of Adjusted Results for Dichotomous Variables – Model 2 (Ranch Hands: Log_2 (Initial Dioxin))

Table Ref.	Clinical Parameter	Adj. Relative Risk (95% C.I.)	p-Value
9-3	Self-perception of Health	0.98 (0.79,1.21)	0.832
9-4	Appearance of Illness or Distress	0.65 (0.36,1.15)	0.117
9-5	Relative Age Appearance	1.01 (0.77,1.31)	0.962
9-7	Body Fat	1.00 (0.85,1.19)	0.986
9-9	Erythrocyte Sedimentation Rate	1.23 (0.94,1.62)	0.138
10-3	Skin Neoplasms	0.81 (0.68,0.98)	0.028
10-4	Malignant Skin Neoplasms	0.87 (0.68,1.12)	0.287
10-5	Benign Skin Neoplasms	0.79 (0.64,0.97)	0.020
10-6	Skin Neoplasms of Uncertain Behavior or Unspecified Nature	0.88 (0.42,1.85)	0.732
10-7	Basal Cell Carcinoma (All Sites Combined)	0.70 (0.53,0.94)	0.014
10-8	Basal Cell Carcinoma (Ear, Face, Head, and Neck)	0.62 (0.44,0.87)	0.003
10-9	Basal Cell Carcinoma (Trunk)	1.18 (0.75,1.86)	0.470
10-10	Basal Cell Carcinoma (Upper Extremities)	0.56 (0.21,1.51)	0.219
10-11	Basal Cell Carcinoma (Lower Extremities)	1.46 (0.50,4.26)	0.511
10-12	Squamous Cell Carcinoma	0.98 (0.52,1.85)	0.944
10-13	Nonmelanoma	0.79 (0.60,1.03)	0.075
10-14	Melanoma	1.28 (0.76,2.16)	0.366
10-15	Systemic Neoplasms (All Sites Combined)	1.00 (0.84,1.20)	0.980
10-16	Malignant Systemic Neoplasms	0.82 (0.57,1.18)	0.272
10-17	Benign Systemic Neoplasms	0.99 (0.82,1.19)	0.903
10-18	Systemic Neoplasms of Uncertain Behavior or Unspecified Nature	1.16 (0.58,2.31)	0.678
10-19	Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck)	0.79 (0.27,2.33)	0.666
10-20	Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx)	1.15 (0.34,3.88)	0.822
10-21	Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum)	--	--
10-22	Malignant Systemic Neoplasms (Thyroid Gland)	0.12 (0.01,2.84)	0.059
10-23	Malignant Systemic Neoplasms (Bronchus and Lung)	0.53 (0.21,1.34)	0.144
10-24	Malignant Systemic Neoplasms (Liver)	2.06 (0.82,5.15)	0.140
10-25	Malignant Systemic Neoplasms (Colon and Rectum)	0.93 (0.42,2.07)	0.855
10-26	Malignant Systemic Neoplasms (Kidney and Bladder)	1.05 (0.47,2.38)	0.899
10-27	Malignant Systemic Neoplasms (Prostate)	0.68 (0.33,1.37)	0.254
10-28	Malignant Systemic Neoplasms (Testicles)	0.77 (0.22,2.64)	0.663
10-29	Malignant Systemic Neoplasms (Connective and Other Soft Tissues)	2.39 (0.68,8.37)	0.179
10-30	Hodgkin's Disease	--	--
10-31	Non-Hodgkin's Lymphoma	--	--
10-32	Other Malignant Systemic Neoplasms of Lymphoid and Histiocytic Tissue	--	--
10-33	All Malignant Skin and Systemic Neoplasms	0.91 (0.72,1.14)	0.396
10-34	All Skin and Systemic Neoplasms	0.90 (0.76,1.07)	0.244
10-36	PSA	0.61 (0.40,0.93)	0.014
11-3	Inflammatory Diseases	0.98 (0.45,2.17)	0.964
11-4	Hereditary and Degenerative Disorders	1.02 (0.76,1.36)	0.909
11-5	Peripheral Disorders	1.09 (0.90,1.32)	0.400
11-6	Other Neurological Disorders	0.99 (0.81,1.20)	0.922
11-7	Smell	0.83 (0.46,1.50)	0.534
11-8	Visual Fields	4.37 (0.84,22.64)	0.049
11-9	Light Reaction	--	--

Table G-18. Summary of Adjusted Results for Dichotomous Variables – Model 2 (Ranch Hands: Log₂ (Initial Dioxin)) (Continued)

Table Ref.	Clinical Parameter	Adj. Relative Risk (95% C.I.)	p-Value
11-10	Ocular Movement	0.74 (0.40,1.36)	0.318
11-11	Facial Sensation	0.55 (0.06,5.38)	0.553
11-12	Jaw Clench	0.59 (0.08,4.24)	0.562
11-13	Smile	1.50 (0.75,3.02)	0.274
11-14	Palpebral Fissure	1.25 (0.54,2.93)	0.613
11-15	Balance	1.65 (0.61,4.45)	0.350
11-16	Speech	0.19 (0.02,2.32)	0.078
11-17	Tongue Position Relative to Midline	0.59 (0.08,4.24)	0.562
11-18	Palate and Uvula Movement	0.59 (0.08,4.24)	0.562
11-19	Cranial Nerve Index	0.75 (0.53,1.08)	0.110
11-20	Neck Range of Motion	0.91 (0.74,1.13)	0.411
11-21	Pinprick	1.29 (0.92,1.81)	0.134
11-22	Light Touch	1.01 (0.65,1.59)	0.956
11-23	Muscle Status	0.95 (0.64,1.41)	0.792
11-24	Patellar Reflex	1.81 (1.10,2.99)	0.019
11-25	Achilles Reflex	1.22 (0.98,1.51)	0.075
11-26	Biceps Reflex	0.87 (0.44,1.70)	0.675
11-27	Babinski Reflex	1.08 (0.34,3.42)	0.896
11-29	Polyneuropathy Prevalence Index	1.30 (1.03,1.65)	0.029
11-30	Multiple Polyneuropathy Index	1.85 (1.20,2.87)	0.004
11-31	Confirmed Polyneuropathy Indicator	1.98 (1.19,3.29)	0.008
11-32	Tremor	1.02 (0.73,1.44)	0.893
11-33	Coordination	1.18 (0.62,2.24)	0.632
11-34	Romberg Sign	1.65 (0.61,4.45)	0.350
11-35	Gait	1.12 (0.79,1.60)	0.530
11-36	CNS Index	1.03 (0.80,1.33)	0.840
12-3	Psychoses	0.82 (0.55,1.23)	0.338
12-4	Alcohol Dependence	1.04 (0.77,1.42)	0.790
12-5	Drug Dependence	--	--
12-6	Anxiety	0.91 (0.76,1.09)	0.302
12-7	Other Neuroses	0.88 (0.74,1.05)	0.164
12-8	SCL-90-R Anxiety	0.73 (0.57,0.95)	0.016
12-9	SCL-90-R Depression	0.84 (0.67,1.06)	0.138
12-10	SCL-90-R Hostility	0.94 (0.71,1.25)	0.692
12-11	SCL-90-R Interpersonal Sensitivity	0.78 (0.62,0.97)	0.026
12-12	SCL-90-R Obsessive-Compulsive Behavior	0.89 (0.17,1.11)	0.286
12-13	SCL-90-R Paranoid Ideation	0.88 (0.66,1.17)	0.374
12-14	SCL-90-R Phobic Anxiety	0.89 (0.70,1.12)	0.315
12-15	SCL-90-R Psychoticism	0.98 (0.78,1.22)	0.838
12-16	SCL-90-R Somatization	0.76 (0.62,0.94)	0.010
12-17	SCL-90-R Global Severity Index (GSI)	0.86 (0.69,1.06)	0.157
12-18	SCL-90-R Positive Symptom Total (PST)	0.82 (0.66,1.02)	0.067
12-19	SCL-90-R Positive Symptom Distress Index (PSDI)	0.80 (0.61,1.05)	0.107
13-3	Uncharacterized Hepatitis	1.02 (0.58,1.79)	0.936
13-4	Jaundice	1.01 (0.20,5.08)	0.995
13-5	Chronic Liver Disease and Cirrhosis (Alcohol-related)	1.06 (0.72,1.57)	0.765
13-6	Chronic Liver Disease and Cirrhosis (Non-alcohol-related)	1.04 (0.61,1.76)	0.897
13-7	Liver Abscess and Sequelae of Chronic Liver Disease	2.09 (0.61,7.19)	0.277
13-8	Enlarged Liver (Hepatomegaly)	0.91 (0.46,1.80)	0.790

Table G-18. Summary of Adjusted Results for Dichotomous Variables – Model 2 (Ranch Hands: Log2 (Initial Dioxin)) (Continued)

Table Ref.	Clinical Parameter	Adj. Relative Risk (95% C.I.)	p-Value
13-9	Other Liver Disorders	1.23 (1.03,1.47)	0.022
13-10	Current Hepatomegaly	0.66 (0.30,1.45)	0.279
13-12	AST	1.13 (0.86,1.50)	0.380
13-14	ALT	1.32 (1.00,1.73)	0.049
13-16	GGT	1.06 (0.82,1.37)	0.669
13-18	Alkaline Phosphatase	1.04 (0.61,1.76)	0.897
13-20	Total Bilirubin	0.75 (0.46,1.13)	0.154
13-21	Direct Bilirubin	--	--
13-23	Lactic Dehydrogenase	0.98 (0.74.1.30)	0.889
13-25	Cholesterol	1.23 (0.99,1.52)	0.062
13-27	HDL Cholesterol	0.72 (0.53,0.98)	0.029
13-29	Cholesterol-HDL Ratio	1.08 (0.91,1.28)	0.378
13-31	Triglycerides	0.96 (0.80,1.15)	0.690
13-33	Creatine Phosphokinase	1.09 (0.82,1.45)	0.542
13-35	Serum Amylase	1.04 (0.63,1.71)	0.884
13-36	Antibodies for Hepatitis A	1.02 (0.86,1.22)	0.813
13-37	Evidence of Prior Hepatitis B	0.95 (0.74,1.22)	0.669
13-38	Current Hepatitis B	0.39 (0.02,9.42)	0.497
13-39	Antibodies for Hepatitis C	0.63 (0.23,1.75)	0.344
13-40	Stool Hemoccult	0.97 (0.62,1.51)	0.880
13-42	Prealbumin	1.76 (0.94,3.30)	0.081
13-44	Albumin	--	--
13-46	α-1-Acid Glycoprotein	0.92 (0.63,1.35)	0.684
13-50	α-2-Macroglobulin	1.48 (0.96,2.27)	0.072
13-52	Apolipoprotein B	1.06 (0.90,1.25)	0.456
13-54	C3 Complement	1.01 (0.39,2.62)	0.977
13-56	C4 Complement	--	--
13-58	Haptoglobin	0.98 (0.82,1.16)	0.785
13-60	Transferrin	0.93 (0.69,1.24)	0.615
14-3	Essential Hypertension	1.10 (0.91,1.32)	0.314
14-4	Heart Disease (Excluding Essential Hypertension)	0.90 (0.75,1.08)	0.249
14-5	Myocardial Infarction	1.30 (0.95,1.77)	0.106
14-6	Stroke or Transient Ischemia Attack	1.33 (0.72,2.47)	0.379
14-8	Systolic Blood Pressure	0.89 (0.71,1.11)	0.296
14-10	Diastolic Blood Pressure	1.15 (0.80,1.67)	0.446
14-11	Heart Sounds	1.28 (0.83,1.98)	0.266
14-12	Overall Electrocardiograph	1.14 (0.93,1.39)	0.200
14-13	Right Bundle Branch Block	1.12 (0.62,2.04)	0.707
14-14	Left Bundle Branch Block	--	--
14-15	Non-Specific ST- and T-Wave Changes	1.15 (0.91,1.44)	0.237
14-16	Bradycardia	0.98 (0.44,2.22)	0.971
14-17	Tachycardia	--	--
14-18	Arrhythmia	1.00 (0.68,1.48)	0.981
14-19	Evidence of Prior Myocardial Infarction	1.84 (1.13,2.99)	0.012
14-20	ECG: Other Diagnoses	--	--
14-21	Funduscopic Examination	1.14 (0.87,1.50)	0.342
14-22	Carotid Bruits	1.15 (0.62,2.11)	0.658
14-23	Radial Pulses	--	--
14-24	Femoral Pulses	1.17 (0.61,2.24)	0.641

Table G-18. Summary of Adjusted Results for Dichotomous Variables – Model 2 (Ranch Hands: Log_2 (Initial Dioxin)) (Continued)

Table Ref.	Clinical Parameter	Adj. Relative Risk (95% C.I.)	p-Value
14-25	Popliteal Pulses	0.97 (0.53,1.78)	0.924
14-26	Dorsalis Pedis Pulses	1.11 (0.78,1.57)	0.561
14-27	Posterior Tibial Pulses	1.16 (0.81,1.65)	0.417
14-28	Leg Pulses	1.13 (0.84,1.51)	0.433
14-29	Peripheral Pulses	1.06 (0.79,1.41)	0.718
14-30	ICVI Index	1.12 (0.73,1.72)	0.604
15-14	Prothrombin Time	0.72 (0.28,1.85)	0.470
15-15	RBC Morphology	1.02 (0.76,1.38)	0.878
15-18	Absolute Neutrophils (bands) (Zero vs. Nonzero)	0.87 (0.70,1.09)	0.214
15-22	Absolute Eosinophils (Zero vs. Nonzero)	0.92 (0.73,1.18)	0.521
15-24	Absolute Basophils (Zero vs. Nonzero)	0.81 (0.68,0.95)	0.012
16-3	Past Thyroid Disease	1.20 (0.88,1.64)	0.245
16-4	Composite Diabetes Indicator	1.36 (1.09,1.69)	0.005
16-7	Thyroid Gland	1.01 (0.32,3.17)	0.981
16-8	Testicular Examination	1.08 (0.72,1.61)	0.714
16-12	Thyroxine	1.51 (0.87,2.62)	0.143
16-13	Anti-Thyroid Antibodies	1.01 (0.31,3.23)	0.990
16-15	Fasting Glucose	1.31 (1.06,1.62)	0.013
16-17	2-Hour Postprandial Glucose	0.99 (0.76,1.29)	0.940
16-18	Fasting Urinary Glucose	1.27 (0.90,1.79)	0.173
16-19	2-Hour Postprandial Urinary Glucose	0.94 (0.75,1.17)	0.585
16-23	α-1-C Hemoglobin	1.53 (1.19,1.96)	0.001
16-25	Total Testosterone	1.16 (0.87,1.55)	0.307
16-27	Free Testosterone	0.41 (0.14,1.18)	0.051
16-29	Estradiol	1.12 (0.94,1.33)	0.213
16-31	LH	0.97 (0.65,1.43)	0.873
16-33	FSH	1.11 (0.81,1.53)	0.508
17-14	ANA Test	1.04 (0.88,1.24)	0.622
17-15	ANA Thyroid Microsomal Antibody	0.77 (0.43,1.35)	0.344
17-16	MSK Smooth Muscle Antibody	0.77 (0.58,1.04)	0.082
17-17	MSK Mitochondrial Antibody	0.10 (0.01,4.01)	0.049
17-18	MSK Parietal Antibody	0.93 (0.64,1.35)	0.694
17-19	Rheumatoid Factor	0.83 (0.60,1.14)	0.233
18-3	Asthma	1.22 (0.82,1.82)	0.328
18-4	Bronchitis	1.07 (0.88,1.30)	0.510
18-5	Pneumonia	0.85 (0.63,1.14)	0.274
18-6	Thorax and Lung Abnormalities	1.14 (0.86,1.51)	0.366
18-7	X-ray Interpretation	0.95 (0.71,1.27)	0.730

--: Relative risk, confidence interval, and p-value are not presented because of the sparse number of Ranch Hands with abnormalities.

Note: Relative risk for a twofold increase in initial dioxin.

Table G-19. Summary of Adjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category)

Table Ref.	Clinical Parameter	Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value
9-3	Self-perception of Health	Comparison	1,211		
		Background RH	376	1.13 (0.75,1.72)	0.555
		Low RH	237	1.62 (1.08,2.44)	0.020
		High RH	240	1.86 (1.26,2.74)	0.002
		Low plus High RH	477	1.74 (1.27,2.37)	0.001
9-4	Appearance of Illness or Distress	Comparison	1,211		
		Background RH	378	0.76 (0.21,2.80)	0.684
		Low RH	237	2.31 (0.87,6.11)	0.092
		High RH	241	1.67 (0.54,5.19)	0.372
		Low plus High RH	478	1.96 (0.84,4.58)	0.118
9-5	Relative Age Appearance	Comparison	1,211		
		Background RH	378	1.42 (0.93,2.16)	0.102
		Low RH	237	1.11 (0.67,1.82)	0.691
		High RH	241	1.05 (0.65,1.69)	0.857
		Low plus High RH	478	1.08 (0.74,1.57)	0.706
9-7	Body Fat	Comparison	1,211		
		Background RH	378	0.60 (0.45,0.80)	0.001
		Low RH	237	1.31 (0.97,1.77)	0.073
		High RH	241	1.12 (0.83,1.53)	0.451
		Low plus High RH	478	1.21 (0.97,1.53)	0.097
9-9	Erythrocyte Sedimentation Rate	Comparison	1,211		
		Background RH	376	1.07 (0.66,1.73)	0.777
		Low RH	237	1.04 (0.61,1.75)	0.897
		High RH	240	1.36 (0.82,2.26)	0.237
		Low plus High RH	477	1.19 (0.80,1.77)	0.398
10-3	Skin Neoplasms	Comparison	1,131		
		Background RH	358	1.46 (1.13,1.88)	0.004
		Low RH	210	1.49 (1.10,2.04)	0.011
		High RH	229	1.05 (0.76,1.45)	0.747
		Low plus High RH	439	1.25 (0.98,1.58)	0.073
10-4	Malignant Skin Neoplasms	Comparison	1,131		
		Background RH	358	1.13 (0.81,1.58)	0.476
		Low RH	210	1.45 (0.98,2.14)	0.062
		High RH	229	1.19 (0.76,1.85)	0.453
		Low plus High RH	439	1.30 (0.95,1.80)	0.104
10-5	Benign Skin Neoplasms	Comparison	1,200		
		Background RH	377	1.64 (1.25,2.15)	<0.001
		Low RH	233	1.21 (0.87,1.69)	0.265
		High RH	242	0.95 (0.67,1.36)	0.798
		Low plus High RH	475	1.07 (0.82,1.39)	0.603

Table G-19. Summary of Adjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value
10-6	Skin Neoplasms of Uncertain Behavior or Unspecified Nature	Comparison	1,131		
		Background RH	358	0.92 (0.18,4.75)	0.921
		Low RH	210	1.91 (0.47,7.69)	0.363
		High RH	229	0.89 (0.18,4.41)	0.889
		Low plus High RH	439	1.28 (0.40,4.14)	0.675
10-7	Basal Cell Carcinoma (All Sites Combined)	Comparison	1,131		
		Background RH	358	1.16 (0.81,1.65)	0.427
		Low RH	210	1.59 (1.06,2.39)	0.026
		High RH	229	0.99 (0.60,1.64)	0.979
		Low plus High RH	439	1.24 (0.88,1.77)	0.223
10-8	Basal Cell Carcinoma (Ear, Face, Head, and Neck)	Comparison	1,131		
		Background RH	358	1.19 (0.80,1.77)	0.386
		Low RH	210	1.54 (0.98,2.42)	0.061
		High RH	229	0.95 (0.54,1.67)	0.846
		Low plus High RH	439	1.19 (0.80,1.77)	0.379
10-9	Basal Cell Carcinoma (Trunk)	Comparison	1,131		
		Background RH	358	0.99 (0.55,1.79)	0.984
		Low RH	210	1.60 (0.83,3.11)	0.161
		High RH	229	1.46 (0.63,3.36)	0.374
		Low plus High RH	439	1.53 (0.85,2.73)	0.153
10-10	Basal Cell Carcinoma (Upper Extremities)	Comparison	1,131		
		Background RH	358	0.74 (0.36,1.52)	0.416
		Low RH	210	0.93 (0.39,2.21)	0.876
		High RH	229	0.64 (0.18,2.23)	0.484
		Low plus High RH	439	0.77 (0.34,1.71)	0.518
10-11	Basal Cell Carcinoma (Lower Extremities)	Comparison	1,131		
		Background RH	358	1.89 (0.43,8.34)	0.398
		Low RH	210	0.90 (0.10,8.17)	0.928
		High RH	229	1.03 (0.12,9.27)	0.976
		Low plus High RH	439	0.97 (0.18,5.16)	0.971
10-12	Squamous Cell Carcinoma	Comparison	1,131		
		Background RH	358	1.53 (0.68,3.45)	0.306
		Low RH	210	1.52 (0.56,4.10)	0.408
		High RH	229	1.74 (0.53,5.69)	0.363
		Low plus High RH	439	1.63 (0.69,3.82)	0.262
10-13	Nonmelanoma	Comparison	1,131		
		Background RH	358	1.16 (0.82,1.64)	0.398
		Low RH	210	1.43 (0.96,2.13)	0.081
		High RH	229	1.06 (0.67,1.69)	0.803
		Low plus High RH	439	1.22 (0.88,1.71)	0.235
10-14	Melanoma	Comparison	1,131		
		Background RH	358	1.56 (0.59,4.16)	0.373
		Low RH	210	2.17 (0.73,6.48)	0.164
		High RH	229	2.71 (0.76,9.67)	0.124
		Low plus High RH	439	2.44 (0.96,6.23)	0.062

Table G-19. Summary of Adjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value
10-15	Systemic Neoplasms (All Sites Combined)	Comparison	1,202		
		Background RH	373	0.76 (0.57,1.03)	0.076
		Low RH	230	0.98 (0.70,1.38)	0.927
		High RH	239	0.95 (0.67,1.36)	0.794
		Low plus High RH	469	0.97 (0.73,1.28)	0.823
10-16	Malignant Systemic Neoplasms	Comparison	1,209		
		Background RH	375	0.73 (0.42,1.29)	0.279
		Low RH	232	1.94 (1.16,3.24)	0.012
		High RH	240	0.86 (0.41,1.78)	0.680
		Low plus High RH	472	1.28 (0.77,2.13)	0.345
10-17	Benign Systemic Neoplasms	Comparison	1,202		
		Background RH	373	0.89 (0.66,1.22)	0.479
		Low RH	230	0.86 (0.60,1.23)	0.400
		High RH	239	1.00 (0.69,1.45)	0.996
		Low plus High RH	469	0.93 (0.69,1.24)	0.613
10-18	Systemic Neoplasms of Uncertain Behavior or Unspecified Nature	Comparison	1,209		
		Background RH	375	0.72 (0.30,1.76)	0.475
		Low RH	232	0.85 (0.32,2.26)	0.744
		High RH	240	0.40 (0.09,1.89)	0.250
		Low plus High RH	472	0.58 (0.22,1.58)	0.288
10-19	Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck)	Comparison	1,209		
		Background RH	375	0.64 (0.16,2.59)	0.533
		Low RH	232	1.94 (0.58,6.44)	0.281
		High RH	240	0.49 (0.06,4.31)	0.520
		Low plus High RH	472	0.96 (0.24,3.82)	0.956
10-20	Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx)	Comparison	1,209		
		Background RH	375	0.39 (0.04,3.56)	0.401
		Low RH	232	1.01 (0.18,5.59)	0.987
		High RH	240	0.56 (0.06,5.33)	0.614
		Low plus High RH	472	0.75 (0.16,3.59)	0.719
10-21	Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum)	Comparison			
		Background RH		--	--
		Low RH		--	--
		High RH		--	--
		Low plus High RH		--	--
10-22	Malignant Systemic Neoplasms (Thyroid Gland)	Comparison	1,209		
		Background RH	375	--	--
		Low RH	232	5.18 (0.71,37.60)	0.104
		High RH	240	--	--
		Low plus High RH	472	--	--
10-23	Malignant Systemic Neoplasms (Bronchus and Lung)	Comparison	1,209		
		Background RH	375	1.52 (0.21,11.09)	0.678
		Low RH	232	8.67 (1.74,43.23)	0.008
		High RH	240	--	--
		Low plus High RH	472	--	--

Table G-19. Summary of Adjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value
10-24	Malignant Systemic Neoplasms (Liver)	Comparison	1,209		
		Background RH	375	--	--
		Low RH	232	--	--
		High RH	240	7.06 (0.70,71.25)	0.098
		Low plus High RH	472	--	--
10-25	Malignant Systemic Neoplasms (Colon and Rectum)	Comparison	1,209		
		Background RH	375	0.60 (0.06,5.76)	0.658
		Low RH	232	3.28 (0.77,13.90)	0.107
		High RH	240	0.57 (0.05,5.85)	0.632
		Low plus High RH	472	1.34 (0.27,6.56)	0.717
10-26	Malignant Systemic Neoplasms (Kidney and Bladder)	Comparison	1,209		
		Background RH	375	2.26 (0.49,10.35)	0.292
		Low RH	232	4.44 (1.04,18.95)	0.044
		High RH	240	3.26 (0.46,23.17)	0.237
		Low plus High RH	472	3.80 (0.88,16.46)	0.075
10-27	Malignant Systemic Neoplasms (Prostate)	Comparison	1,209		
		Background RH	375	0.48 (0.21,1.07)	0.072
		Low RH	232	0.91 (0.42,1.97)	0.818
		High RH	240	0.61 (0.19,1.93)	0.404
		Low plus High RH	472	0.75 (0.35,1.60)	0.453
10-28	Malignant Systemic Neoplasms (Testicles)	Comparison			
		Background RH		--	--
		Low RH		--	--
		High RH		--	--
		Low plus High RH		--	--
10-29	Malignant Systemic Neoplasms (Connective and Other Soft Tissues)	Comparison	1,209		
		Background RH	375	--	--
		Low RH	232	--	--
		High RH	240	3.17 (0.17,57.71)	0.436
		Low plus High RH	472	--	--
10-30	Hodgkin's Disease	Comparison	1,209		
		Background RH	375	0.55 (0.05,6.15)	0.624
		Low RH	232	--	--
		High RH	240	--	--
		Low plus High RH	472	--	--
10-31	Non-Hodgkin's Lymphoma	Comparison	1,209		
		Background RH	375	0.24 (0.01,4.90)	0.351
		Low RH	232	--	--
		High RH	240	--	--
		Low plus High RH	472	--	--
10-32	Other Malignant Systemic Neoplasms of Lymphoid and Histiocytic Tissue	Comparison	1,209		
		Background RH	375	1.90 (0.15,23.45)	0.618
		Low RH	232	--	--
		High RH	240	--	--
		Low plus High RH	472	--	--

Table G-19. Summary of Adjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value
10-33	All Malignant Skin and Systemic Neoplasms	Comparison	1,196		
		Background RH	372	0.84 (0.60,1.20)	0.339
		Low RH	226	1.51 (1.03,2.21)	0.035
		High RH	239	1.01 (0.66,1.57)	0.952
		Low plus High RH	465	1.23 (0.88,1.71)	0.221
10-34	All Skin and Systemic Neoplasms	Comparison	1,189		
		Background RH	371	1.01 (0.76,1.33)	0.956
		Low RH	225	1.15 (0.83,1.61)	0.396
		High RH	238	0.93 (0.67,1.30)	0.684
		Low plus High RH	463	1.04 (0.79,1.35)	0.799
10-36	PSA	Comparison	1,151		
		Background RH	362	0.76 (0.43,1.37)	0.368
		Low RH	221	1.42 (0.79,2.56)	0.246
		High RH	234	1.04 (0.51,2.16)	0.907
		Low plus High RH	455	1.21 (0.71,2.08)	0.484
11-3	Inflammatory Diseases	Comparison	1,203		
		Background RH	377	13.28 (1.31,135.01)	0.029
		Low RH	238	13.85 (1.20,160.07)	0.035
		High RH	238	12.43 (1.03,149.42)	0.047
		Low plus High RH	476	13.12 (1.39,123.67)	0.024
11-4	Hereditary and Degenerative Diseases	Comparison	1,193		
		Background RH	375	1.16 (0.77,1.76)	0.474
		Low RH	235	0.92 (0.56,1.52)	0.736
		High RH	236	1.01 (0.61,1.67)	0.979
		Low plus High RH	471	0.96 (0.65,1.41)	0.841
11-5	Peripheral Disorders	Comparison	1,191		
		Background RH	372	0.88 (0.64,1.21)	0.437
		Low RH	235	1.25 (0.89,1.76)	0.190
		High RH	236	1.33 (0.94,1.90)	0.111
		Low plus High RH	471	1.29 (0.99,1.69)	0.059
11-6	Other Neurological Disorders	Comparison	1,188		
		Background RH	372	1.21 (0.85,1.73)	0.281
		Low RH	235	1.31 (0.90,1.89)	0.161
		High RH	235	1.23 (0.85,1.77)	0.271
		Low plus High RH	470	1.27 (0.95,1.69)	0.106
11-7	Smell	Comparison	1,191		
		Background RH	373	1.04 (0.40,2.73)	0.929
		Low RH	234	1.57 (0.61,4.06)	0.353
		High RH	235	0.82 (0.23,2.92)	0.758
		Low plus High RH	469	1.13 (0.48,2.68)	0.777
11-8	Visual Fields	Comparison	1,189		
		Background RH	375	0.86 (0.10,7.83)	0.897
		Low RH	235	--	--
		High RH	236	0.57 (0.06,5.52)	0.629
		Low plus High RH	471	--	--

Table G-19. Summary of Adjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value
11-9	Light Reaction	Comparison	1,191		
		Background RH	371	0.38 (0.05,3.03)	0.359
		Low RH	235	--	--
		High RH	235	--	--
		Low plus High RH	470	--	--
11-10	Ocular Movement	Comparison	1,193		
		Background RH	375	1.18 (0.37,3.73)	0.781
		Low RH	235	1.76 (0.61,5.07)	0.291
		High RH	236	1.32 (0.45,3.83)	0.614
		Low plus High RH	471	1.52 (0.65,3.55)	0.328
11-11	Facial Sensation	Comparison	1,209		
		Background RH	376	1.70 (0.14,19.96)	0.672
		Low RH	238	2.04 (0.18,23.31)	0.564
		High RH	238	--	--
		Low plus High RH	476	--	--
11-12	Jaw Clench	Comparison			
		Background RH		--	--
		Low RH		--	--
		High RH		--	--
		Low plus High RH		--	--
11-13	Smile	Comparison	1,210		
		Background RH	377	3.14 (0.65,15.08)	0.152
		Low RH	238	2.38 (0.42,13.43)	0.326
		High RH	238	1.80 (0.30,10.67)	0.517
		Low plus High RH	476	2.07 (0.50,8.57)	0.315
11-14	Palpebral Fissure	Comparison	1,210		
		Background RH	377	0.96 (0.26,3.60)	0.955
		Low RH	238	0.79 (0.17,3.64)	0.761
		High RH	238	0.35 (0.04,2.84)	0.324
		Low plus High RH	476	0.52 (0.13,2.05)	0.352
11-15	Balance	Comparison	1,192		
		Background RH	375	2.54 (0.74,8.72)	0.138
		Low RH	235	0.63 (0.08,5.24)	0.667
		High RH	236	0.63 (0.07,5.49)	0.672
		Low plus High RH	471	0.63 (0.13,3.11)	0.567
11-16	Speech	Comparison	1,193		
		Background RH	375	1.09 (0.22,5.46)	0.919
		Low RH	235	1.38 (0.28,6.71)	0.688
		High RH	236	--	--
		Low plus High RH	471	--	--
11-17	Tongue Position Relative to Midline	Comparison			
		Background RH		--	--
		Low RH		--	--
		High RH		--	--
		Low plus High RH		--	--

Table G-19. Summary of Adjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value
11-18	Palate and Uvula Movement	Comparison			
		Background RH		--	--
		Low RH		--	--
		High RH		--	--
		Low plus High RH		--	--
11-19	Cranial Nerve Index	Comparison	1,189		
		Background RH	366	1.20 (0.72,2.02)	0.484
		Low RH	232	1.29 (0.74,2.24)	0.369
		High RH	232	0.60 (0.30,1.22)	0.158
		Low plus High RH	464	0.88 (0.54,1.43)	0.604
11-20	Neck Range of Motion	Comparison	1,193		
		Background RH	375	1.12 (0.80,1.57)	0.523
		Low RH	235	1.60 (1.12,2.29)	0.010
		High RH	236	1.55 (1.05,2.29)	0.028
		Low plus High RH	471	1.57 (1.18,2.11)	0.002
11-21	Pinprick	Comparison	1,132		
		Background RH	357	1.11 (0.63,1.95)	0.716
		Low RH	222	0.95 (0.51,1.77)	0.868
		High RH	223	1.55 (0.88,2.73)	0.126
		Low plus High RH	445	1.21 (0.77,1.93)	0.410
11-22	Light Touch	Comparison	1,132		
		Background RH	357	1.07 (0.54,2.10)	0.852
		Low RH	222	1.12 (0.55,2.27)	0.751
		High RH	223	1.09 (0.53,2.26)	0.808
		Low plus High RH	445	1.11 (0.64,1.93)	0.718
11-23	Muscle Status	Comparison	1,192		
		Background RH	375	1.22 (0.63,2.35)	0.550
		Low RH	235	1.90 (0.98,3.66)	0.056
		High RH	236	1.58 (0.73,3.39)	0.242
		Low plus High RH	471	1.73 (0.99,3.04)	0.056
11-24	Patellar Reflex	Comparison	1,191		
		Background RH	375	0.88 (0.40,1.91)	0.742
		Low RH	234	0.86 (0.37,2.02)	0.737
		High RH	236	1.39 (0.60,3.26)	0.446
		Low plus High RH	470	1.10 (0.57,2.10)	0.778
11-25	Achilles Reflex	Comparison	1,188		
		Background RH	374	0.96 (0.68,1.35)	0.811
		Low RH	235	0.97 (0.66,1.42)	0.880
		High RH	236	1.32 (0.89,1.95)	0.168
		Low plus High RH	471	1.13 (0.84,1.52)	0.416
11-26	Biceps Reflex	Comparison	1,192		
		Background RH	375	0.27 (0.03,2.13)	0.213
		Low RH	235	2.52 (0.95,6.70)	0.064
		High RH	236	1.37 (0.35,5.29)	0.651
		Low plus High RH	471	1.85 (0.73,4.69)	0.193

Table G-19. Summary of Adjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value
11-27	Babinski Reflex	Comparison	1,190		
		Background RH	375	1.53 (0.45,5.14)	0.496
		Low RH	235	0.38 (0.05,3.05)	0.364
		High RH	236	0.41 (0.05,3.33)	0.405
		Low plus High RH	471	0.40 (0.08,1.85)	0.239
11-29	Polyneuropathy Prevalence Index	Comparison	1,130		
		Background RH	356	0.83 (0.57,1.20)	0.315
		Low RH	222	0.86 (0.57,1.30)	0.484
		High RH	223	1.31 (0.86,1.98)	0.206
		Low plus High RH	445	1.06 (0.77,1.46)	0.708
11-30	Multiple Polyneuropathy Index	Comparison	1,130		
		Background RH	356	1.37 (0.69,2.72)	0.366
		Low RH	222	0.96 (0.44,2.10)	0.914
		High RH	223	2.38 (1.18,4.82)	0.016
		Low plus High RH	445	1.51 (0.84,2.71)	0.165
11-31	Confirmed Polyneuropathy Indicator	Comparison	1,138		
		Background RH	355	0.99 (0.20,4.97)	0.988
		Low RH	223	1.56 (0.38,6.40)	0.536
		High RH	221	6.04 (1.63,22.42)	0.007
		Low plus High RH	444	3.06 (1.02,9.23)	0.047
11-32	Tremor	Comparison	1,193		
		Background RH	375	1.11 (0.71,1.74)	0.659
		Low RH	235	0.71 (0.39,1.28)	0.248
		High RH	236	0.79 (0.44,1.40)	0.420
		Low plus High RH	471	0.75 (0.48,1.16)	0.194
11-33	Coordination	Comparison	1,191		
		Background RH	375	1.46 (0.71,3.01)	0.298
		Low RH	235	0.61 (0.21,1.79)	0.371
		High RH	236	0.42 (0.12,1.42)	0.161
		Low plus High RH	471	0.51 (0.22,1.19)	0.117
11-34	Romberg Sign	Comparison	1,192		
		Background RH	375	2.54 (0.74,8.72)	0.138
		Low RH	235	0.63 (0.08,5.24)	0.667
		High RH	236	0.63 (0.07,5.49)	0.672
		Low plus High RH	471	0.63 (0.13,3.11)	0.567
11-35	Gait	Comparison	1,193		
		Background RH	375	1.52 (0.90,2.59)	0.121
		Low RH	235	0.77 (0.38,1.57)	0.479
		High RH	236	1.44 (0.76,2.74)	0.262
		Low plus High RH	471	1.06 (0.63,1.78)	0.832
11-36	CNS Index	Comparison	1,192		
		Background RH	375	1.24 (0.86,1.77)	0.249
		Low RH	235	0.67 (0.42,1.09)	0.105
		High RH	236	0.94 (0.60,1.47)	0.789
		Low plus High RH	471	0.80 (0.56,1.13)	0.205

Table G-19. Summary of Adjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value
12-3	Psychoses	Comparison	1,196		
		Background RH	376	0.85 (0.41,1.73)	0.648
		Low RH	236	1.42 (0.73,2.77)	0.297
		High RH	236	0.90 (0.45,1.80)	0.759
		Low plus High RH	472	1.13 (0.67,1.91)	0.647
12-4	Alcohol Dependence	Comparison	1,196		
		Background RH	376	1.04 (0.63,1.69)	0.888
		Low RH	237	1.11 (0.64,1.91)	0.714
		High RH	238	1.01 (0.58,1.73)	0.985
		Low plus High RH	475	1.05 (0.69,1.60)	0.802
12-5	Drug Dependence	Comparison	1,196		
		Background RH	374	1.37 (0.19,9.67)	0.755
		Low RH	236	--	--
		High RH	236	--	--
		Low plus High RH	472	--	--
12-6	Anxiety	Comparison	1,194		
		Background RH	372	0.98 (0.74,1.31)	0.902
		Low RH	235	1.17 (0.85,1.60)	0.343
		High RH	235	0.82 (0.59,1.13)	0.225
		Low plus High RH	470	0.98 (0.77,1.25)	0.857
12-7	Other Neuroses	Comparison	1,187		
		Background RH	367	0.89 (0.69,1.14)	0.368
		Low RH	234	1.37 (1.02,1.84)	0.036
		High RH	233	1.18 (0.87,1.61)	0.286
		Low plus High RH	467	1.27 (1.01,1.60)	0.038
12-8	SCL-90-R Anxiety	Comparison	1,196		
		Background RH	374	0.86 (0.55,1.35)	0.506
		Low RH	236	1.09 (0.69,1.73)	0.717
		High RH	235	0.76 (0.48,1.20)	0.237
		Low plus High RH	471	0.91 (0.64,1.29)	0.595
12-9	SCL-90-R Depression	Comparison	1,196		
		Background RH	374	0.88 (0.60,1.27)	0.485
		Low RH	236	0.78 (0.51,1.20)	0.256
		High RH	235	0.74 (0.49,1.11)	0.142
		Low plus High RH	471	0.76 (0.55,1.04)	0.087
12-10	SCL-90-R Hostility	Comparison	1,196		
		Background RH	374	0.86 (0.52,1.40)	0.536
		Low RH	236	0.80 (0.46,1.40)	0.440
		High RH	235	0.84 (0.51,1.38)	0.488
		Low plus High RH	471	0.82 (0.55,1.22)	0.333
12-11	SCL-90-R Interpersonal Sensitivity	Comparison	1,196		
		Background RH	374	0.73 (0.49,1.07)	0.110
		Low RH	236	0.92 (0.62,1.38)	0.698
		High RH	235	0.77 (0.53,1.14)	0.190
		Low plus High RH	471	0.84 (0.63,1.14)	0.270

Table G-19. Summary of Adjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value
12-12	SCL-90-R Obsessive-Compulsive Behavior	Comparison	1,196		
		Background RH	374	0.84 (0.58,1.21)	0.340
		Low RH	236	1.01 (0.68,1.50)	0.948
		High RH	235	0.72 (0.48,1.07)	0.103
		Low plus High RH	471	0.85 (0.63,1.15)	0.298
12-13	SCL-90-R Paranoid Ideation	Comparison	1,196		
		Background RH	374	0.90 (0.51,1.57)	0.702
		Low RH	236	0.87 (0.47,1.61)	0.657
		High RH	235	1.16 (0.71,1.89)	0.559
		Low plus High RH	471	1.00 (0.65,1.54)	0.990
12-14	SCL-90-R Phobic Anxiety	Comparison	1,196		
		Background RH	374	0.65 (0.40,1.06)	0.086
		Low RH	236	1.04 (0.65,1.67)	0.872
		High RH	235	1.11 (0.72,1.70)	0.647
		Low plus High RH	471	1.07 (0.76,1.52)	0.694
12-15	SCL-90-R Psychoticism	Comparison	1,196		
		Background RH	374	0.71 (0.47,1.07)	0.104
		Low RH	236	0.83 (0.53,1.28)	0.394
		High RH	235	0.95 (0.64,1.40)	0.786
		Low plus High RH	471	0.88 (0.65,1.21)	0.447
12-16	SCL-90-R Somatization	Comparison	1,196		
		Background RH	374	0.92 (0.63,1.34)	0.669
		Low RH	236	1.36 (0.93,1.97)	0.108
		High RH	235	0.92 (0.63,1.33)	0.643
		Low plus High RH	471	1.11 (0.84,1.48)	0.457
12-17	SCL-90-R Global Severity Index (GSI)	Comparison	1,196		
		Background RH	374	0.77 (0.51,1.15)	0.200
		Low RH	236	1.03 (0.69,1.55)	0.877
		High RH	235	0.93 (0.64,1.36)	0.711
		Low plus High RH	471	0.98 (0.73,1.32)	0.897
12-18	SCL-90-R Positive Symptom Total (PST)	Comparison	1,196		
		Background RH	374	0.67 (0.45,0.99)	0.045
		Low RH	236	1.04 (0.71,1.54)	0.830
		High RH	235	0.78 (0.53,1.15)	0.209
		Low plus High RH	471	0.90 (0.67,1.21)	0.496
12-19	SCL-90-R Positive Symptom Distress Index (PSDI)	Comparison	1,196		
		Background RH	374	1.16 (0.70,1.92)	0.572
		Low RH	236	1.31 (0.77,2.23)	0.325
		High RH	235	1.38 (0.85,2.23)	0.191
		Low plus High RH	471	1.34 (0.91,1.99)	0.143
13-3	Uncharacterized Hepatitis	Comparison	1,205		
		Background RH	375	1.39 (0.59,3.27)	0.450
		Low RH	236	1.00 (0.34,2.97)	0.999
		High RH	239	1.04 (0.38,2.89)	0.932
		Low plus High RH	475	1.02 (0.46,2.28)	0.957

Table G-19. Summary of Adjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value
13-4	Jaundice	Comparison	1,181		
		Background RH	367	0.99 (0.49,2.03)	0.988
		Low RH	231	--	--
		High RH	235	0.16 (0.02,1.20)	0.075
		Low plus High RH	466	--	--
13-5	Chronic Liver Disease and Cirrhosis (Alcohol-related)	Comparison	1,146		
		Background RH	358	1.03 (0.56,1.90)	0.914
		Low RH	225	0.95 (0.48,1.91)	0.894
		High RH	219	0.88 (0.43,1.81)	0.734
		Low plus High RH	444	0.92 (0.54,1.57)	0.755
13-6	Chronic Liver Disease and Cirrhosis (Non-alcohol-related)	Comparison	1,211		
		Background RH	378	1.89 (0.68,5.25)	0.223
		Low RH	238	1.15 (0.32,4.12)	0.829
		High RH	241	1.37 (0.47,4.00)	0.568
		Low plus High RH	479	1.26 (0.51,3.12)	0.625
13-7	Liver Abscess and Sequelae of Chronic Liver Disease	Comparison	1,212		
		Background RH	378	--	--
		Low RH	238	--	--
		High RH	241	7.76 (0.38,158.28)	0.183
		Low plus High RH	479	--	--
13-8	Enlarged Liver (Hepatomegaly)	Comparison	1,210		
		Background RH	378	0.80 (0.32,2.01)	0.630
		Low RH	238	0.35 (0.08,1.51)	0.159
		High RH	240	1.09 (0.42,2.79)	0.864
		Low plus High RH	478	0.62 (0.25,1.54)	0.302
13-9	Other Liver Disorders	Comparison	1,201		
		Background RH	375	1.13 (0.86,1.49)	0.371
		Low RH	237	1.05 (0.76,1.45)	0.757
		High RH	241	1.52 (1.11,2.08)	0.009
		Low plus High RH	478	1.27 (1.00,1.62)	0.055
13-10	Current Hepatomegaly	Comparison	1,193		
		Background RH	374	1.64 (0.40,6.69)	0.489
		Low RH	235	2.26 (0.57,9.01)	0.247
		High RH	239	2.62 (0.70,9.84)	0.154
		Low plus High RH	474	2.44 (0.82,7.24)	0.109
13-12	AST	Comparison	1,193		
		Background RH	374	0.70 (0.40,1.22)	0.212
		Low RH	235	1.28 (0.75,2.18)	0.360
		High RH	238	1.79 (1.08,2.96)	0.024
		Low plus High RH	473	1.51 (1.02,2.26)	0.041
13-14	ALT	Comparison	1,193		
		Background RH	374	0.71 (0.41,1.23)	0.223
		Low RH	235	1.30 (0.77,2.18)	0.323
		High RH	238	1.53 (0.95,2.45)	0.080
		Low plus High RH	473	1.41 (0.96,2.07)	0.079

Table G-19. Summary of Adjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value
13-16	GGT	Comparison	1,193		
		Background RH	374	0.77 (0.48,1.23)	0.273
		Low RH	235	1.42 (0.91,2.22)	0.127
		High RH	238	1.35 (0.86,2.11)	0.186
		Low plus High RH	473	1.38 (0.98,1.95)	0.065
13-18	Alkaline Phosphatase	Comparison	1,193		
		Background RH	375	1.85 (0.88,3.90)	0.104
		Low RH	235	0.91 (0.31,2.71)	0.871
		High RH	239	1.23 (0.44,3.41)	0.688
		Low plus High RH	474	1.06 (0.48,2.37)	0.883
13-20	Total Bilirubin	Comparison	1,193		
		Background RH	374	0.88 (0.53,1.47)	0.619
		Low RH	235	1.03 (0.58,1.84)	0.919
		High RH	238	0.59 (0.27,1.27)	0.175
		Low plus High RH	473	0.78 (0.47,1.29)	0.331
13-21	Direct Bilirubin	Comparison	1,193		
		Background RH	374	1.09 (0.12,10.31)	0.937
		Low RH	235	--	--
		High RH	238	--	--
		Low plus High RH	473	--	--
13-23	Lactic Dehydrogenase	Comparison	1,191		
		Background RH	374	1.07 (0.72,1.61)	0.729
		Low RH	235	0.80 (0.48,1.31)	0.366
		High RH	238	0.81 (0.49,1.34)	0.416
		Low plus High RH	473	0.80 (0.55,1.17)	0.255
13-25	Cholesterol	Comparison	1,193		
		Background RH	374	0.85 (0.60,1.21)	0.379
		Low RH	235	1.01 (0.68,1.51)	0.964
		High RH	238	1.41 (0.97,2.04)	0.071
		Low plus High RH	473	1.19 (0.89,1.60)	0.240
13-27	HDL Cholesterol	Comparison	1,192		
		Background RH	374	1.57 (1.00,2.45)	0.049
		Low RH	234	1.09 (0.64,1.84)	0.761
		High RH	238	0.80 (0.47,1.37)	0.416
		Low plus High RH	472	0.93 (0.62,1.40)	0.731
13-29	Cholesterol-HDL Ratio	Comparison	1,192		
		Background RH	374	1.00 (0.77,1.28)	0.982
		Low RH	234	0.83 (0.61,1.12)	0.221
		High RH	238	1.26 (0.93,1.69)	0.133
		Low plus High RH	472	1.02 (0.82,1.28)	0.849
13-31	Triglycerides	Comparison	1,193		
		Background RH	373	0.79 (0.56,1.10)	0.161
		Low RH	235	1.24 (0.88,1.76)	0.215
		High RH	238	1.55 (1.12,2.15)	0.009
		Low plus High RH	473	1.39 (1.07,1.80)	0.012

Table G-19. Summary of Adjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value
13-33	Creatine Phosphokinase	Comparison	1,193		
		Background RH	374	0.75 (0.46,1.20)	0.227
		Low RH	235	0.80 (0.47,1.35)	0.402
		High RH	238	1.20 (0.73,1.98)	0.465
		Low plus High RH	473	0.98 (0.67,1.45)	0.923
13-35	Serum Amylase	Comparison	1,193		
		Background RH	374	0.53 (0.24,1.16)	0.112
		Low RH	235	1.37 (0.67,2.77)	0.387
		High RH	238	1.02 (0.41,2.59)	0.959
		Low plus High RH	473	1.18 (0.63,2.21)	0.602
13-36	Antibodies for Hepatitis A	Comparison	1,211		
		Background RH	378	0.92 (0.70,1.21)	0.561
		Low RH	238	0.92 (0.67,1.25)	0.577
		High RH	241	0.96 (0.70,1.32)	0.787
		Low plus High RH	479	0.94 (0.74,1.19)	0.588
13-37	Evidence of Prior Hepatitis B	Comparison	1,210		
		Background RH	378	0.50 (0.31,0.80)	0.004
		Low RH	237	0.71 (0.45,1.12)	0.143
		High RH	241	0.59 (0.37,0.92)	0.021
		Low plus High RH	478	0.65 (0.46,0.91)	0.012
13-38	Current Hepatitis B	Comparison	1,212		
		Background RH	378	--	--
		Low RH	238	1.94 (0.14,26.64)	0.622
		High RH	241	--	--
		Low plus High RH	479	--	--
13-39	Antibodies for Hepatitis C	Comparison	1,212		
		Background RH	378	0.87 (0.28,2.73)	0.816
		Low RH	238	0.54 (0.12,2.40)	0.415
		High RH	241	0.50 (0.11,2.23)	0.359
		Low plus High RH	479	0.52 (0.17,1.57)	0.243
13-40	Stool Hemoccult	Comparison	1,161		
		Background RH	363	0.63 (0.31,1.28)	0.201
		Low RH	231	1.08 (0.55,2.13)	0.822
		High RH	230	0.86 (0.39,1.90)	0.705
		Low plus High RH	461	0.96 (0.55,1.68)	0.895
13-42	Prealbumin	Comparison	1,193		
		Background RH	374	1.74 (0.61,5.01)	0.302
		Low RH	235	0.49 (0.06,3.93)	0.506
		High RH	238	4.34 (1.25,15.05)	0.021
		Low plus High RH	473	1.48 (0.41,5.32)	0.552
13-44	Albumin	Comparison	1,193		
		Background RH	374	0.67 (0.14,3.20)	0.611
		Low RH	235	--	--
		High RH	238	--	--
		Low plus High RH	473	--	--

Table G-19. Summary of Adjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value
13-46	α-1-Acid Glycoprotein	Comparison	1,193		
		Background RH	374	1.12 (0.58,2.16)	0.745
		Low RH	235	1.47 (0.73,2.94)	0.279
		High RH	238	1.54 (0.77,3.08)	0.222
		Low plus High RH	473	1.50 (0.88,2.58)	0.138
13-50	α-2-Macroglobulin	Comparison	1,193		
		Background RH	374	0.45 (0.19,1.10)	0.079
		Low RH	235	0.61 (0.27,1.40)	0.246
		High RH	238	1.09 (0.51,2.31)	0.823
		Low plus High RH	473	0.82 (0.45,1.49)	0.511
13-52	Apolipoprotein B	Comparison	1,193		
		Background RH	374	0.79 (0.62,1.00)	0.050
		Low RH	235	0.82 (0.62,1.09)	0.164
		High RH	238	0.97 (0.73,1.30)	0.849
		Low plus High RH	473	0.89 (0.72,1.11)	0.305
13-54	C3 Complement	Comparison	1,193		
		Background RH	374	1.25 (0.61,2.57)	0.536
		Low RH	235	0.21 (0.03,1.57)	0.128
		High RH	238	0.49 (0.11,2.17)	0.351
		Low plus High RH	473	0.32 (0.09,1.16)	0.083
13-56	C4 Complement	Comparison	1,193		
		Background RH	374	2.99 (0.40,22.39)	0.286
		Low RH	235	--	--
		High RH	238	--	--
		Low plus High RH	473	--	--
13-58	Haptoglobin	Comparison	1,193		
		Background RH	374	1.32 (1.01,1.72)	0.042
		Low RH	235	1.25 (0.92,1.69)	0.160
		High RH	238	1.15 (0.84,1.56)	0.382
		Low plus High RH	473	1.19 (0.95,1.51)	0.136
13-60	Transferrin	Comparison	1,193		
		Background RH	374	0.73 (0.48,1.11)	0.142
		Low RH	235	0.78 (0.49,1.26)	0.311
		High RH	238	0.57 (0.32,0.99)	0.045
		Low plus High RH	473	0.66 (0.45,0.98)	0.039
14-3	Essential Hypertension	Comparison	1,145		
		Background RH	356	0.87 (0.66,1.14)	0.320
		Low RH	217	0.87 (0.63,1.20)	0.395
		High RH	235	1.27 (0.93,1.74)	0.131
		Low plus High RH	452	1.06 (0.84,1.35)	0.624
14-4	Heart Disease (Excluding Essential Hypertension)	Comparison	1,155		
		Background RH	360	1.34 (1.03,1.75)	0.032
		Low RH	221	1.33 (0.96,1.84)	0.081
		High RH	236	1.03 (0.76,1.40)	0.865
		Low plus High RH	457	1.16 (0.92,1.48)	0.209

Table G-19. Summary of Adjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value
14-5	Myocardial Infarction	Comparison	1,155		
		Background RH	360	0.89 (0.55,1.43)	0.625
		Low RH	221	0.84 (0.49,1.46)	0.544
		High RH	236	1.39 (0.83,2.32)	0.215
		Low plus High RH	457	1.09 (0.73,1.63)	0.673
14-6	Stroke or Transient Ischemia Attack	Comparison	1,155		
		Background RH	360	0.97 (0.30,3.16)	0.956
		Low RH	221	0.42 (0.05,3.26)	0.404
		High RH	236	2.65 (0.83,8.46)	0.100
		Low plus High RH	457	1.08 (0.32,3.71)	0.900
14-8	Systolic Blood Pressure	Comparison	1,155		
		Background RH	360	1.00 (0.73,1.37)	0.983
		Low RH	221	1.12 (0.79,1.59)	0.532
		High RH	236	0.84 (0.57,1.23)	0.365
		Low plus High RH	457	0.96 (0.73,1.27)	0.791
14-10	Diastolic Blood Pressure	Comparison	1,155		
		Background RH	360	0.78 (0.41,1.48)	0.449
		Low RH	221	0.91 (0.45,1.83)	0.792
		High RH	236	1.46 (0.80,2.68)	0.221
		Low plus High RH	457	1.16 (0.71,1.91)	0.551
14-11	Heart Sounds	Comparison	1,155		
		Background RH	360	0.45 (0.21,0.97)	0.041
		Low RH	221	0.80 (0.39,1.61)	0.528
		High RH	236	1.05 (0.52,2.11)	0.901
		Low plus High RH	457	0.92 (0.54,1.56)	0.750
14-12	Overall Electrocardiograph	Comparison	1,155		
		Background RH	360	1.00 (0.76,1.32)	0.980
		Low RH	221	0.73 (0.52,1.02)	0.063
		High RH	236	1.10 (0.78,1.54)	0.578
		Low plus High RH	457	0.90 (0.70,1.16)	0.423
14-13	Right Bundle Branch Block	Comparison	1,155		
		Background RH	360	1.04 (0.47,2.29)	0.920
		Low RH	221	0.55 (0.19,1.60)	0.273
		High RH	236	1.19 (0.49,2.88)	0.704
		Low plus High RH	457	0.82 (0.39,1.71)	0.594
14-14	Left Bundle Branch Block	Comparison	1,155		
		Background RH	360	0.87 (0.23,3.33)	0.838
		Low RH	221	0.37 (0.05,2.91)	0.341
		High RH	236	--	--
		Low plus High RH	457	--	--
14-15	Non-Specific ST- and T-Wave Changes	Comparison	1,155		
		Background RH	360	0.82 (0.58,1.15)	0.242
		Low RH	221	0.91 (0.62,1.32)	0.614
		High RH	236	1.26 (0.86,1.84)	0.238
		Low plus High RH	457	1.07 (0.80,1.43)	0.628

Table G-19. Summary of Adjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value
14-16	Bradycardia	Comparison	1,155		
		Background RH	360	0.81 (0.44,1.49)	0.497
		Low RH	221	0.49 (0.17,1.40)	0.183
		High RH	236	0.35 (0.08,1.50)	0.156
		Low plus High RH	457	0.41 (0.16,1.05)	0.062
14-17	Tachycardia	Comparison	1,155		
		Background RH	360	2.01 (0.16,24.61)	0.585
		Low RH	221	--	--
		High RH	236	8.10 (1.19,55.01)	0.032
		Low plus High RH	457	--	--
14-18	Arrhythmia	Comparison	1,155		
		Background RH	360	0.87 (0.49,1.57)	0.647
		Low RH	221	1.17 (0.65,2.11)	0.596
		High RH	236	1.10 (0.56,2.12)	0.774
		Low plus High RH	457	1.13 (0.70,1.83)	0.604
14-19	Evidence of Prior Myocardial Infarction	Comparison	1,155		
		Background RH	360	0.69 (0.34,1.37)	0.285
		Low RH	221	0.79 (0.39,1.61)	0.524
		High RH	236	1.11 (0.52,2.36)	0.783
		Low plus High RH	457	0.94 (0.54,1.65)	0.841
14-20	ECG: Other Diagnoses	Comparison	1,186		
		Background RH	368	2.89 (0.16,52.97)	0.474
		Low RH	227	--	--
		High RH	239	12.41 (1.00,154.15)	0.050
		Low plus High RH	466	--	--
14-21	Funduscopic Examination	Comparison	1,154		
		Background RH	359	1.04 (0.70,1.55)	0.842
		Low RH	221	0.82 (0.52,1.30)	0.402
		High RH	236	0.95 (0.60,1.51)	0.836
		Low plus High RH	457	0.89 (0.63,1.26)	0.500
14-22	Carotid Bruits	Comparison	1,155		
		Background RH	360	1.06 (0.47,2.38)	0.893
		Low RH	221	0.69 (0.25,1.86)	0.460
		High RH	236	1.01 (0.41,2.45)	0.991
		Low plus High RH	457	0.84 (0.41,1.71)	0.625
14-23	Radial Pulses	Comparison	1,155		
		Background RH	360	3.27 (0.64,16.71)	0.155
		Low RH	221	3.82 (0.53,27.51)	0.183
		High RH	236	1.26 (0.11,14.89)	0.856
		Low plus High RH	457	2.15 (0.36,13.04)	0.404
14-24	Femoral Pulses	Comparison	1,154		
		Background RH	360	1.22 (0.44,3.36)	0.702
		Low RH	221	1.71 (0.58,4.98)	0.329
		High RH	236	2.45 (0.76,7.90)	0.134
		Low plus High RH	457	2.06 (0.85,4.96)	0.108

Table G-19. Summary of Adjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value
14-25	Popliteal Pulses	Comparison	1,153		
		Background RH	360	0.88 (0.37,2.05)	0.760
		Low RH	221	1.15 (0.45,2.92)	0.776
		High RH	236	1.08 (0.40,2.86)	0.884
		Low plus High RH	457	1.11 (0.53,2.30)	0.781
14-26	Dorsalis Pedis Pulses	Comparison	1,153		
		Background RH	360	0.94 (0.59,1.50)	0.792
		Low RH	221	0.99 (0.58,1.70)	0.977
		High RH	236	0.89 (0.50,1.58)	0.685
		Low plus High RH	457	0.94 (0.61,1.43)	0.761
14-27	Posterior Tibial Pulses	Comparison	1,151		
		Background RH	360	1.08 (0.62,1.89)	0.784
		Low RH	221	1.31 (0.71,2.39)	0.387
		High RH	236	1.21 (0.63,2.30)	0.571
		Low plus High RH	457	1.25 (0.77,2.03)	0.358
14-28	Leg Pulses	Comparison	1,151		
		Background RH	360	1.01 (0.66,1.53)	0.981
		Low RH	221	1.01 (0.63,1.64)	0.955
		High RH	236	0.91 (0.54,1.53)	0.725
		Low plus High RH	457	0.96 (0.66,1.40)	0.832
14-29	Peripheral Pulses	Comparison	1,151		
		Background RH	360	1.00 (0.66,1.52)	0.997
		Low RH	221	1.05 (0.65,1.70)	0.833
		High RH	236	0.94 (0.57,1.57)	0.828
		Low plus High RH	457	1.00 (0.68,1.45)	0.981
14-30	ICVI Index	Comparison	1,155		
		Background RH	360	0.69 (0.32,1.48)	0.340
		Low RH	221	0.98 (0.46,2.11)	0.968
		High RH	236	1.41 (0.69,2.89)	0.346
		Low plus High RH	457	1.19 (0.67,2.09)	0.555
15-14	Prothrombin Time	Comparison	986		
		Background RH	308	1.41 (0.52,3.85)	0.501
		Low RH	182	1.01 (0.28,3.71)	0.984
		High RH	193	0.49 (0.06,3.96)	0.502
		Low plus High RH	375	0.70 (0.19,2.57)	0.586
15-15	RBC Morphology	Comparison	1,210		
		Background RH	380	1.18 (0.72,1.93)	0.517
		Low RH	238	1.39 (0.84,2.30)	0.206
		High RH	239	1.08 (0.60,1.94)	0.800
		Low plus High RH	477	1.22 (0.80,1.86)	0.352
15-18	Absolute Neutrophils (Zero vs. Nonzero) (bands)	Comparison	1,210		
		Background RH	380	1.02 (0.75,1.40)	0.897
		Low RH	238	1.03 (0.72,1.49)	0.859
		High RH	239	0.88 (0.59,1.30)	0.515
		Low plus High RH	477	0.95 (0.72,1.27)	0.741

Table G-19. Summary of Adjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value
15-22	Absolute Eosinophils (Zero vs. Nonzero)	Comparison	1,210		
		Background RH	380	1.07 (0.74,1.55)	0.705
		Low RH	238	1.16 (0.77,1.76)	0.467
		High RH	239	0.82 (0.53,1.27)	0.376
		Low plus High RH	477	0.98 (0.71,1.35)	0.885
15-24	Absolute Basophils (Zero vs. Nonzero)	Comparison	1,210		
		Background RH	380	1.11 (0.87,1.41)	0.395
		Low RH	238	1.47 (1.10,1.95)	0.009
		High RH	239	1.00 (0.75,1.33)	0.979
		Low plus High RH	477	1.21 (0.97,1.50)	0.091
16-3	Thyroid Disease	Comparison	1,208		
		Background RH	376	0.92 (0.60,1.42)	0.707
		Low RH	237	0.70 (0.40,1.22)	0.209
		High RH	240	1.07 (0.64,1.81)	0.792
		Low plus High RH	477	0.87 (0.57,1.30)	0.490
16-4	Composite Diabetes Indicator	Comparison	1,183		
		Background RH	375	0.69 (0.46,1.02)	0.065
		Low RH	232	1.22 (0.83,1.79)	0.311
		High RH	238	1.47 (1.00,2.17)	0.048
		Low plus High RH	470	1.34 (1.00,1.80)	0.049
16-7	Thyroid Gland	Comparison	1,165		
		Background RH	367	0.65 (0.21,2.01)	0.457
		Low RH	233	0.29 (0.04,2.19)	0.229
		High RH	233	0.56 (0.07,4.62)	0.590
		Low plus High RH	466	0.40 (0.09,1.81)	0.234
16-8	Testicular Examination	Comparison	1,199		
		Background RH	374	0.84 (0.45,1.58)	0.594
		Low RH	237	1.46 (0.78,2.71)	0.236
		High RH	240	1.39 (0.63,3.03)	0.415
		Low plus High RH	477	1.42 (0.82,2.45)	0.207
16-12	Thyroxine	Comparison	1,161		
		Background RH	365	1.23 (0.63,2.42)	0.545
		Low RH	233	0.45 (0.14,1.49)	0.192
		High RH	233	1.53 (0.62,3.73)	0.354
		Low plus High RH	466	0.83 (0.38,1.82)	0.641
16-13	Anti-Thyroid Antibodies	Comparison	1,161		
		Background RH	365	1.07 (0.27,4.26)	0.921
		Low RH	233	0.73 (0.09,5.99)	0.765
		High RH	233	1.07 (0.12,9.66)	0.951
		Low plus High RH	466	0.88 (0.17,4.46)	0.879
16-15	Fasting Glucose	Comparison	1,200		
		Background RH	377	0.91 (0.63,1.31)	0.609
		Low RH	235	1.03 (0.70,1.53)	0.877
		High RH	240	1.44 (0.99,2.11)	0.056
		Low plus High RH	475	1.22 (0.91,1.64)	0.178

Table G-19. Summary of Adjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value
16-17	2-Hour Postprandial Glucose	Comparison	987		
		Background RH	338	0.94 (0.64,1.37)	0.729
		Low RH	183	1.12 (0.73,1.72)	0.616
		High RH	181	1.01 (0.64,1.60)	0.960
		Low plus High RH	364	1.06 (0.76,1.49)	0.722
16-18	Fasting Urinary Glucose	Comparison	1,200		
		Background RH	377	0.63 (0.27,1.43)	0.265
		Low RH	235	0.92 (0.43,1.97)	0.827
		High RH	240	1.33 (0.71,2.49)	0.369
		Low plus High RH	475	1.11 (0.65,1.89)	0.704
16-19	2-Hour Postprandial Urinary Glucose	Comparison	985		
		Background RH	337	1.32 (0.98,1.78)	0.072
		Low RH	182	1.41 (0.98,2.02)	0.064
		High RH	181	0.97 (0.66,1.44)	0.885
		Low plus High RH	363	1.17 (0.88,1.56)	0.283
16-23	α-1-C Hemoglobin	Comparison	1,200		
		Background RH	377	0.84 (0.53,1.35)	0.474
		Low RH	235	0.94 (0.58,1.52)	0.799
		High RH	240	1.76 (1.16,2.67)	0.008
		Low plus High RH	475	1.29 (0.91,1.82)	0.148
16-25	Total Testosterone	Comparison	1,189		
		Background RH	370	0.98 (0.59,1.62)	0.934
		Low RH	234	0.95 (0.55,1.62)	0.841
		High RH	237	1.55 (0.94,2.55)	0.085
		Low plus High RH	471	1.21 (0.82,1.80)	0.340
16-27	Free Testosterone	Comparison	1,189		
		Background RH	370	0.88 (0.32,2.46)	0.811
		Low RH	234	1.38 (0.57,3.35)	0.470
		High RH	237	0.28 (0.04,2.21)	0.227
		Low plus High RH	471	0.62 (0.19,2.01)	0.424
16-29	Estradiol	Comparison	1,213		
		Background RH	381	0.97 (0.75,1.27)	0.842
		Low RH	239	0.79 (0.57,1.09)	0.155
		High RH	243	1.05 (0.77,1.44)	0.757
		Low plus High RH	482	0.91 (0.72,1.16)	0.460
16-31	LH	Comparison	1,213		
		Background RH	381	1.28 (0.79,2.08)	0.313
		Low RH	239	0.83 (0.44,1.58)	0.573
		High RH	243	0.76 (0.36,1.60)	0.475
		Low plus High RH	482	0.80 (0.47,1.34)	0.392
16-33	FSH	Comparison	1,213		
		Background RH	381	1.10 (0.72,1.69)	0.652
		Low RH	239	0.93 (0.55,1.56)	0.781
		High RH	243	1.16 (0.64,2.08)	0.621
		Low plus High RH	482	1.04 (0.68,1.58)	0.859

Table G-19. Summary of Adjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value
17-14	ANA Test	Comparison	1,154		
		Background RH	365	1.04 (0.82,1.33)	0.738
		Low RH	220	0.85 (0.63,1.14)	0.276
		High RH	229	1.15 (0.85,1.55)	0.364
		Low plus High RH	449	0.99 (0.79,1.24)	0.936
17-15	ANA Thyroid Microsomal Antibody	Comparison	1,154		
		Background RH	365	1.03 (0.51,2.12)	0.925
		Low RH	220	1.12 (0.49,2.59)	0.785
		High RH	229	0.81 (0.30,2.16)	0.671
		Low plus High RH	449	0.95 (0.48,1.90)	0.883
17-16	MSK Smooth Muscle Antibody	Comparison	1,154		
		Background RH	365	1.28 (0.90,1.83)	0.173
		Low RH	220	1.07 (0.70,1.65)	0.752
		High RH	229	0.59 (0.36,1.00)	0.048
		Low plus High RH	449	0.79 (0.55,1.14)	0.209
17-17	MSK Mitochondrial Antibody	Comparison	1,154		
		Background RH	365	3.55 (0.48,26.04)	0.213
		Low RH	220	4.30 (0.57,32.27)	0.156
		High RH	229	--	--
		Low plus High RH	449	--	--
17-18	MSK Parietal Antibody	Comparison	1,154		
		Background RH	365	0.63 (0.30,1.31)	0.216
		Low RH	220	1.50 (0.82,2.75)	0.192
		High RH	229	0.97 (0.47,1.99)	0.928
		Low plus High RH	449	1.20 (0.72,2.00)	0.490
17-19	Rheumatoid Factor	Comparison	1,154		
		Background RH	365	1.04 (0.71,1.51)	0.841
		Low RH	220	1.03 (0.66,1.61)	0.890
		High RH	229	0.59 (0.33,1.04)	0.068
		Low plus High RH	449	0.77 (0.53,1.14)	0.195
18-3	Asthma	Comparison	1,207		
		Background RH	376	1.52 (0.86,2.70)	0.149
		Low RH	234	1.13 (0.54,2.36)	0.753
		High RH	240	1.29 (0.64,2.61)	0.479
		Low plus High RH	474	1.21 (0.69,2.10)	0.506
18-4	Bronchitis	Comparison	1,187		
		Background RH	371	1.31 (0.98,1.75)	0.073
		Low RH	227	0.94 (0.65,1.36)	0.734
		High RH	239	1.10 (0.78,1.56)	0.584
		Low plus High RH	466	1.02 (0.78,1.34)	0.891
18-5	Pneumonia	Comparison	1,167		
		Background RH	360	0.90 (0.61,1.33)	0.602
		Low RH	221	0.98 (0.63,1.54)	0.929
		High RH	236	0.74 (0.44,1.25)	0.265
		Low plus High RH	457	0.85 (0.59,1.23)	0.386

Table G-19. Summary of Adjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value
18-6	Thorax and Lung Abnormalities	Comparison	1,212		
		Background RH	380	0.84 (0.55,1.28)	0.412
		Low RH	238	1.01 (0.63,1.62)	0.953
		High RH	243	1.01 (0.62,1.64)	0.977
		Low plus High RH	481	1.01 (0.70,1.46)	0.955
18-7	X-ray Interpretation	Comparison	1,212		
		Background RH	380	1.69 (1.18,2.43)	0.004
		Low RH	238	1.11 (0.70,1.75)	0.657
		High RH	241	0.66 (0.38,1.13)	0.127
		Low plus High RH	479	0.85 (0.58,1.24)	0.406

--: Relative risk, confidence interval, and p-value are not presented because of the sparse number of participants with abnormalities.

Note: Relative risk and confidence interval relative to Comparisons.
RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background: (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table G-20. Summary of Adjusted Results for Dichotomous Variables – Model 4 (Ranch Hands: Log_2 (1987 Dioxin + 1))

Table Ref.	Clinical Parameter	Adj. Relative Risk (95% C.I.)	p-Value
9-3	Self-perception of Health	1.14 (0.98,1.32)	0.079
9-4	Appearance of Illness or Distress	1.05 (0.72,1.52)	0.800
9-5	Relative Age Appearance	0.89 (0.75,1.05)	0.153
9-7	Body Fat	1.29 (1.14,1.46)	<0.001
9-9	Erythrocyte Sedimentation Rate	1.14 (0.94,1.38)	0.169
10-3	Skin Neoplasms	0.92 (0.82,1.03)	0.147
10-4	Malignant Skin Neoplasms	1.06 (0.91,1.25)	0.447
10-5	Benign Skin Neoplasms	0.84 (0.74,0.95)	0.005
10-6	Skin Neoplasms of Uncertain Behavior or Unspecified Nature	1.11 (0.69,1.81)	0.664
10-7	Basal Cell Carcinoma (All Sites Combined)	0.99 (0.83,1.18)	0.924
10-8	Basal Cell Carcinoma (Ear, Face, Head, and Neck)	0.89 (0.74,1.09)	0.257
10-9	Basal Cell Carcinoma (Trunk)	1.51 (1.07,2.13)	0.016
10-10	Basal Cell Carcinoma (Upper Extremities)	1.00 (0.63,1.57)	0.987
10-11	Basal Cell Carcinoma (Lower Extremities)	0.91 (0.42,1.98)	0.803
10-12	Squamous Cell Carcinoma	1.07 (0.70,1.63)	0.749
10-13	Nonmelanoma	1.02 (0.86,1.21)	0.786
10-14	Melanoma	1.18 (0.81,1.71)	0.399
10-15	Systemic Neoplasms (All Sites Combined)	1.05 (0.93,1.18)	0.399
10-16	Malignant Systemic Neoplasms	1.06 (0.84,1.34)	0.599
10-17	Benign Systemic Neoplasms	1.01 (0.89,1.14)	0.905
10-18	Systemic Neoplasms of Uncertain Behavior or Unspecified Nature	1.07 (0.67,1.72)	0.767
10-19	Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck)	1.04 (0.57,1.91)	0.897
10-20	Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx)	1.60 (0.65,3.97)	0.296
10-21	Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum)	0.31 (0.09,1.04)	0.017
10-22	Malignant Systemic Neoplasms (Thyroid Gland)	0.95 (0.34,2.70)	0.925
10-23	Malignant Systemic Neoplasms (Bronchus and Lung)	1.15 (0.63,2.11)	0.638
10-24	Malignant Systemic Neoplasms (Liver)	2.52 (1.03,6.15)	0.042
10-25	Malignant Systemic Neoplasms (Colon and Rectum)	1.44 (0.72,2.86)	0.291
10-26	Malignant Systemic Neoplasms (Kidney and Bladder)	1.14 (0.66,1.96)	0.634
10-27	Malignant Systemic Neoplasms (Prostate)	0.83 (0.56,1.23)	0.353
10-28	Malignant Systemic Neoplasms (Testicles)	1.35 (0.54,3.37)	0.517
10-29	Malignant Systemic Neoplasms (Connective and Other Soft Tissues)	2.36 (0.72,7.79)	0.155
10-30	Hodgkin's Disease	0.70 (0.08,6.51)	0.745
10-31	Non-Hodgkin's Lymphoma	0.31 (0.01,7.88)	0.443
10-32	Other Malignant Systemic Neoplasms of Lymphoid and Histiocytic Tissue	0.63 (0.09,4.17)	0.580
10-33	All Malignant Skin and Systemic Neoplasms	1.10 (0.94,1.27)	0.227
10-34	All Skin and Systemic Neoplasms	0.99 (0.88,1.11)	0.854
10-36	PSA	1.05 (0.81,1.35)	0.735
11-3	Inflammatory Diseases	0.90 (0.52,1.57)	0.716
11-4	Hereditary and Degenerative Disorders	0.92 (0.77,1.11)	0.380
11-5	Peripheral Disorders	1.20 (1.04,1.38)	0.011
11-6	Other Neurological Disorders	0.97 (0.84,1.11)	0.625
11-7	Smell	0.83 (0.56,1.22)	0.333
11-8	Visual Fields	1.40 (0.58,3.38)	0.456
11-9	Light Reaction	0.75 (0.18,3.12)	0.681

Table G-20. Summary of Adjusted Results for Dichotomous Variables – Model 4 (Ranch Hands: Log_2 (1987 Dioxin + 1)) (Continued)

Table Ref.	Clinical Parameter	Adj. Relative Risk (95% C.I.)	p-Value
11-10	Ocular Movement	0.91 (0.63,1.32)	0.614
11-11	Facial Sensation	0.79 (0.23,2.66)	0.694
11-12	Jaw Clench	1.02 (0.34,3.08)	0.969
11-13	Smile	0.99 (0.59,1.65)	0.972
11-14	Palpebral Fissure	1.17 (0.65,2.12)	0.598
11-15	Balance	0.95 (0.52,1.73)	0.860
11-16	Speech	0.73 (0.36,1.47)	0.370
11-17	Tongue Position Relative to Midline	1.02 (0.34,3.08)	0.969
11-18	Palate and Uvula Movement	1.19 (0.32,4.46)	0.800
11-19	Cranial Nerve Index	0.88 (0.71,1.10)	0.254
11-20	Neck Range of Motion	1.09 (0.94,1.26)	0.267
11-21	Pinprick	1.12 (0.88,1.42)	0.345
11-22	Light Touch	1.01 (0.75,1.36)	0.940
11-23	Muscle Status	0.98 (0.76,1.27)	0.897
11-24	Patellar Reflex	1.15 (0.80,1.64)	0.447
11-25	Achilles Reflex	1.12 (0.96,1.31)	0.157
11-26	Biceps Reflex	1.52 (0.89,2.61)	0.120
11-27	Babinski Reflex	0.65 (0.33,1.29)	0.223
11-29	Polyneuropathy Prevalence Index	1.16 (0.98,1.37)	0.080
11-30	Multiple Polyneuropathy Index	1.29 (0.95,1.76)	0.101
11-31	Confirmed Polyneuropathy Indicator	2.21 (1.24,3.96)	0.003
11-32	Tremor	0.93 (0.75,1.14)	0.478
11-33	Coordination	0.83 (0.57,1.21)	0.330
11-34	Romberg Sign	0.95 (0.52,1.73)	0.860
11-35	Gait	0.99 (0.78,1.25)	0.905
11-36	CNS Index	0.94 (0.80,1.10)	0.443
12-3	Psychoses	1.08 (0.84,1.40)	0.550
12-4	Alcohol Dependence	0.99 (0.82,1.20)	0.898
12-5	Drug Dependence	0.45 (0.10,2.11)	0.226
12-6	Anxiety	0.95 (0.84,1.07)	0.368
12-7	Other Neuroses	1.02 (0.91,1.14)	0.763
12-8	SCL-90-R Anxiety	0.96 (0.81,1.13)	0.619
12-9	SCL-90-R Depression	0.97 (0.84,1.13)	0.712
12-10	SCL-90-R Hostility	1.01 (0.84,1.23)	0.889
12-11	SCL-90-R Interpersonal Sensitivity	0.95 (0.82,1.10)	0.511
12-12	SCL-90-R Obsessive-Compulsive Behavior	1.00 (0.87,1.16)	0.964
12-13	SCL-90-R Paranoid Ideation	1.00 (0.82,1.20)	0.960
12-14	SCL-90-R Phobic Anxiety	1.03 (0.88,1.21)	0.727
12-15	SCL-90-R Psychoticism	1.06 (0.91,1.23)	0.484
12-16	SCL-90-R Somatization	0.95 (0.83,1.09)	0.458
12-17	SCL-90-R Global Severity Index (GSI)	1.04 (0.90,1.21)	0.555
12-18	SCL-90-R Positive Symptom Total (PST)	1.02 (0.89,1.18)	0.764
12-19	SCL-90-R Positive Symptom Distress Index (PSDI)	0.96 (0.81,1.15)	0.675
13-3	Uncharacterized Hepatitis	0.78 (0.55,1.12)	0.184
13-4	Jaundice	0.39 (0.24,0.65)	<0.001
13-5	Chronic Liver Disease and Cirrhosis (Alcohol-related)	1.09 (0.84,1.41)	0.506
13-6	Chronic Liver Disease and Cirrhosis (Non-alcohol-related)	1.02 (0.68,1.54)	0.920
13-7	Liver Abscess and Sequelae of Chronic Liver Disease	2.05 (0.68,6.15)	0.212
13-8	Enlarged Liver (Hepatomegaly)	0.93 (0.60,1.46)	0.753

Table G-20. Summary of Adjusted Results for Dichotomous Variables – Model 4 (Ranch Hands: Log₂ (1987 Dioxin + 1)) (Continued)

Table Ref.	Clinical Parameter	Adj. Relative Risk (95% C.I.)	p-Value
13-9	Other Liver Disorders	1.11 (0.99,1.25)	0.077
13-10	Current Hepatomegaly	1.05 (0.64,1.74)	0.838
13-12	AST	1.38 (1.12,1.71)	0.002
13-14	ALT	1.48 (1.20,1.83)	<0.001
13-16	GGT	1.27 (1.05,1.53)	0.012
13-18	Alkaline Phosphatase	0.69 (0.50,0.94)	0.020
13-20	Total Bilirubin	0.94 (0.73,1.21)	0.646
13-21	Direct Bilirubin	0.79 (0.17,3.72)	0.764
13-23	Lactic Dehydrogenase	1.01 (0.84,1.21)	0.892
13-25	Cholesterol	1.08 (0.93,1.24)	0.312
13-27	HDL Cholesterol	0.82 (0.68,0.98)	0.029
13-29	Cholesterol-HDL Ratio	1.13 (1.01,1.26)	0.025
13-31	Triglycerides	1.23 (1.09,1.40)	0.001
13-33	Creatine Phosphokinase	1.22 (1.00,1.49)	0.043
13-35	Serum Amylase	0.93 (0.68,1.26)	0.623
13-36	Antibodies for Hepatitis A	1.06 (0.94,1.19)	0.346
13-37	Evidence of Prior Hepatitis B	1.06 (0.89,1.25)	0.531
13-38	Current Hepatitis B	1.33 (0.27,6.59)	0.719
13-39	Antibodies for Hepatitis C	0.67 (0.40,1.14)	0.141
13-40	Stool Hemoccult	1.13 (0.83,1.53)	0.448
13-42	Prealbumin	1.00 (0.63,1.60)	0.993
13-44	Albumin	0.52 (0.09,3.01)	0.442
13-46	α-1-Acid Glycoprotein	0.87 (0.68,1.11)	0.261
13-50	α-2-Macroglobulin	1.50 (1.08,2.08)	0.014
13-52	Apolipoprotein B	1.07 (0.96,1.18)	0.242
13-54	C3 Complement	0.57 (0.39,0.84)	0.004
13-56	C4 Complement	0.26 (0.08,0.86)	0.024
13-58	Haptoglobin	0.91 (0.82,1.02)	0.107
13-60	Transferrin	1.03 (0.85,1.24)	0.785
14-3	Essential Hypertension	1.18 (1.04,1.34)	0.011
14-4	Heart Disease (Excluding Essential Hypertension)	0.92 (0.81,1.04)	0.159
14-5	Myocardial Infarction	1.16 (0.94,1.44)	0.170
14-6	Stroke or Transient Ischemia Attack	1.15 (0.71,1.85)	0.578
14-8	Systolic Blood Pressure	0.88 (0.76,1.02)	0.099
14-10	Diastolic Blood Pressure	1.20 (0.89,1.61)	0.228
14-11	Heart Sounds	1.24 (0.89,1.73)	0.193
14-12	Overall Electrocardiograph	1.02 (0.89,1.17)	0.753
14-13	Right Bundle Branch Block	1.02 (0.69,1.50)	0.922
14-14	Left Bundle Branch Block	0.56 (0.23,1.39)	0.199
14-15	Non-Specific ST- and T-Wave Changes	1.12 (0.95,1.32)	0.180
14-16	Bradycardia	0.98 (0.65,1.49)	0.932
14-17	Tachycardia	1.55 (0.85,2.84)	0.165
14-18	Arrhythmia	1.12 (0.85,1.49)	0.422
14-19	Evidence of Prior Myocardial Infarction	1.33 (0.95,1.87)	0.089
14-20	ECG: Other Diagnoses	1.47 (0.58,3.73)	0.413
14-21	Funduscopic Examination	1.03 (0.85,1.24)	0.767
14-22	Carotid Bruits	0.94 (0.65,1.36)	0.755
14-23	Radial Pulses	0.61 (0.30,1.21)	0.140
14-24	Femoral Pulses	1.29 (0.83,2.03)	0.255

Table G-20. Summary of Adjusted Results for Dichotomous Variables – Model 4 (Ranch Hands: Log₂ (1987 Dioxin + 1)) (Continued)

Table Ref.	Clinical Parameter	Adj. Relative Risk (95% C.I.)	p-Value
14-25	Popliteal Pulses	1.02 (0.72,1.46)	0.908
14-26	Dorsalis Pedis Pulses	1.07 (0.85,1.33)	0.580
14-27	Posterior Tibial Pulses	1.12 (0.88,1.43)	0.354
14-28	Leg Pulses	1.08 (0.88,1.31)	0.467
14-29	Peripheral Pulses	1.07 (0.88,1.30)	0.485
14-30	ICVI Index	1.07 (0.79,1.45)	0.666
15-14	Prothrombin Time	0.86 (0.54,1.38)	0.526
15-15	RBC Morphology	1.02 (0.84,1.25)	0.822
15-18	Absolute Neutrophils (bands) (Zero vs. Nonzero)	0.92 (0.80,1.06)	0.264
15-22	Absolute Eosinophils (Zero vs. Nonzero)	0.99 (0.84,1.16)	0.894
15-24	Absolute Basophils (Zero vs. Nonzero)	0.94 (0.84,1.05)	0.257
16-3	Past Thyroid Disease	1.10 (0.89,1.36)	0.358
16-4	Composite Diabetes Indicator	1.43 (1.21,1.68)	<0.001
16-7	Thyroid Gland	1.09 (0.50,2.36)	0.825
16-8	Testicular Examination	1.09 (0.82,1.44)	0.545
16-12	Thyroxine	1.14 (0.79,1.64)	0.487
16-13	Anti-Thyroid Antibodies	0.86 (0.41,1.80)	0.689
16-15	Fasting Glucose	1.25 (1.08,1.46)	0.003
16-17	2-Hour Postprandial Glucose	1.10 (0.91,1.33)	0.332
16-18	Fasting Urinary Glucose	1.47 (1.11,1.94)	0.006
16-19	2-Hour Postprandial Urinary Glucose	0.90 (0.78,1.03)	0.129
16-23	α-1-C Hemoglobin	1.37 (1.15,1.64)	<0.001
16-25	Total Testosterone	1.20 (0.96,1.49)	0.106
16-27	Free Testosterone	0.94 (0.52,1.70)	0.835
16-29	Estradiol	0.99 (0.89,1.12)	0.926
16-31	LH	0.84 (0.66,1.07)	0.154
16-33	FSH	1.16 (0.93,1.45)	0.188
17-14	ANA Test	0.96 (0.86,1.08)	0.512
17-15	ANA Thyroid Microsomal Antibody	0.96 (0.69,1.35)	0.824
17-16	MSK Smooth Muscle Antibody	0.89 (0.75,1.05)	0.155
17-17	MSK Mitochondrial Antibody	0.65 (0.31,1.38)	0.245
17-18	MSK Parietal Antibody	1.22 (0.93,1.60)	0.140
17-19	Rheumatoid Factor	0.86 (0.71,1.04)	0.122
18-3	Asthma	1.06 (0.81,1.37)	0.680
18-4	Bronchitis	0.90 (0.79,1.03)	0.137
18-5	Pneumonia	0.89 (0.73,1.08)	0.229
18-6	Thorax and Lung Abnormalities	1.20 (1.00,1.43)	0.054
18-7	X-ray Interpretation	0.80 (0.67,0.96)	0.015

Note: Relative risk for a twofold increase in 1987 dioxin.

Table G-21. Summary of Adjusted Results for Polytomous Variables – Model 1 (Ranch Hands vs. Comparisons)

Table Ref.	Clinical Parameter	Contrast	Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value
11-28	Polyneuropathy Severity Index	Moderate vs. None or Mild	All	2.32 (1.14,4.73)	0.020
			Officer	1.72 (0.57,5.24)	0.338
			Enlisted Flyer	4.13 (0.83,20.52)	0.083
			Enlisted Groundcrew	2.16 (0.67,7.01)	0.200
		Severe vs. None or Mild	All	5.44 (0.59,50.52)	0.136
			Officer	--	--
			Enlisted Flyer	--	--
			Enlisted Groundcrew	1.64 (0.09,29.24)	0.738
13-48	α-1-Antitrypsin	Low vs. Normal	All	0.81 (0.37,1.78)	0.606
			Officer	1.10 (0.44,2.78)	0.834
			Enlisted Flyer	--	--
			Enlisted Groundcrew	0.47 (0.10,2.34)	0.358
		High vs. Normal	All	2.51 (0.80,7.90)	0.116
			Officer	--	--
			Enlisted Flyer	0.73 (0.08,6.49)	0.778
			Enlisted Groundcrew	2.69 (0.63,11.58)	0.183
15-4	RBC Count	Low vs. Normal	All	1.00 (0.66,1.51)	0.991
			Officer	0.95 (0.52,1.75)	0.869
			Enlisted Flyer	1.97 (0.73,5.29)	0.180
			Enlisted Groundcrew	0.75 (0.37,1.53)	0.426
		High vs. Normal	All	0.58 (0.22,1.54)	0.278
			Officer	0.23 (0.03,1.89)	0.170
			Enlisted Flyer	1.25 (0.17,9.24)	0.830
			Enlisted Groundcrew	0.73 (0.18,2.98)	0.660
15-6	WBC Count	Low vs. Normal	All	1.18 (0.80,1.74)	0.415
			Officer	1.10 (0.62,1.96)	0.754
			Enlisted Flyer	2.12 (0.73,6.09)	0.165
			Enlisted Groundcrew	1.03 (0.55,1.93)	0.923

Table G-21. Summary of Adjusted Results for Polytomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Contrast	Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value
15-6	WBC Count (continued)	High vs. Normal	All	0.93 (0.58,1.51)	0.783
			Officer	0.91 (0.35,2.35)	0.843
			Enlisted Flyer	0.99 (0.37,2.68)	0.985
			Enlisted Groundcrew	0.93 (0.47,1.82)	0.822
15-8	Hemoglobin	Low vs. Normal	All	1.15 (0.81,1.63)	0.433
			Officer	1.25 (0.72,2.19)	0.433
			Enlisted Flyer	1.58 (0.73,3.44)	0.246
			Enlisted Groundcrew	0.90 (0.51,1.58)	0.713
		High vs. Normal	All	0.61 (0.16,2.38)	0.480
			Officer	1.52 (0.21,10.95)	0.675
			Enlisted Flyer	--	--
			Enlisted Groundcrew	--	--
15-10	Hematocrit	Low vs. Normal	All	1.04 (0.59,1.85)	0.886
			Officer	0.95 (0.38,2.36)	0.908
			Enlisted Flyer	1.84 (0.51,6.72)	0.353
			Enlisted Groundcrew	0.85 (0.33,2.18)	0.739
		High vs. Normal	All	0.28 (0.03,2.40)	0.245
			Officer	--	--
			Enlisted Flyer	--	--
			Enlisted Groundcrew	--	--
15-12	Platelet Count	Low vs. Normal	All	0.84 (0.50,1.42)	0.509
			Officer	2.64 (1.15,6.05)	0.022
			Enlisted Flyer	0.10 (0.01,0.79)	0.029
			Enlisted Groundcrew	0.48 (0.19,1.23)	0.127
		High vs. Normal	All	1.13 (0.30,4.27)	0.853
			Officer	0.55 (0.06,5.37)	0.606
			Enlisted Flyer	1.18 (0.07,19.42)	0.906
			Enlisted Groundcrew	2.61 (0.23,29.36)	0.437

Table G-21. ***Summary of Adjusted Results for Polytomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)***

Table Ref.	Clinical Parameter	Contrast	Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value
16-5	Diabetic Severity	No Treatment vs. Nondiabetic	All	1.10 (0.74,1.62)	0.642
			Officer	0.96 (0.50,1.86)	0.902
			Enlisted Flyer	0.71 (0.29,1.72)	0.445
			Enlisted Groundcrew	1.48 (0.83,2.66)	0.185
		Diet Only vs. Nondiabetic	All	1.52 (0.78,2.96)	0.219
			Officer	2.04 (0.69,5.99)	0.195
			Enlisted Flyer	1.09 (0.15,7.93)	0.931
			Enlisted Groundcrew	1.32 (0.51,3.41)	0.572
		Oral Hypoglycemic vs. Nondiabetic	All	0.73 (0.48,1.11)	0.137
			Officer	0.68 (0.33,1.39)	0.288
			Enlisted Flyer	0.75 (0.29,1.91)	0.544
			Enlisted Groundcrew	0.76 (0.41,1.41)	0.384
		Requiring Insulin vs. Nondiabetic	All	2.20 (1.15,4.20)	0.017
			Officer	2.39 (0.92,6.20)	0.074
			Enlisted Flyer	1.22 (0.24,6.24)	0.811
			Enlisted Groundcrew	2.52 (0.88,7.23)	0.084
16-10	TSH	Abnormal Low vs. Normal	All	1.57 (0.63,3.88)	0.332
			Officer	2.78 (0.50,15.33)	0.241
			Enlisted Flyer	2.01 (0.33,12.28)	0.448
			Enlisted Groundcrew	0.88 (0.21,3.71)	0.859
		Abnormal High vs. Normal	All	1.42 (0.89,2.28)	0.140
			Officer	1.18 (0.57,2.44)	0.648
			Enlisted Flyer	0.63 (0.15,2.55)	0.513
			Enlisted Groundcrew	2.11 (1.04,4.28)	0.037
16-21	Serum Insulin	Abnormal Low vs. Normal	All	0.79 (0.58,1.08)	0.143
			Officer	0.76 (0.48,1.22)	0.256
			Enlisted Flyer	0.83 (0.35,1.95)	0.671
			Enlisted Groundcrew	0.81 (0.50,1.33)	0.412

Table G-21. Summary of Adjusted Results for Polytomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Contrast	Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value
16-21	Serum Insulin (continued)	Abnormal High vs. Normal	All	0.96 (0.77,1.21)	0.749
			Officer	1.08 (0.75,1.53)	0.688
			Enlisted Flyer	0.72 (0.41,1.27)	0.257
			Enlisted Groundcrew	0.97 (0.69,1.36)	0.870
18-11	Loss of Vital Capacity	Mild vs. None	All	0.96 (0.69,1.35)	0.832
			Officer	1.09 (0.62,1.90)	0.768
			Enlisted Flyer	0.68 (0.31,1.52)	0.349
			Enlisted Groundcrew	1.00 (0.61,1.63)	0.999
		Moderate or Severe vs. None	All	0.67 (0.31,1.47)	0.324
			Officer	1.42 (0.40,5.00)	0.586
			Enlisted Flyer	0.25 (0.03,2.30)	0.220
			Enlisted Groundcrew	0.52 (0.16,1.70)	0.279
18-12	Obstructive Abnormality	Mild vs. None	All	1.08 (0.88,1.32)	0.449
			Officer	1.38 (1.01,1.89)	0.041
			Enlisted Flyer	0.79 (0.48,1.29)	0.345
			Enlisted Groundcrew	0.96 (0.70,1.32)	0.821
		Moderate vs. None	All	0.97 (0.66,1.44)	0.887
			Officer	1.21 (0.63,2.32)	0.560
			Enlisted Flyer	1.36 (0.57,3.23)	0.492
			Enlisted Groundcrew	0.65 (0.35,1.22)	0.180
		Severe vs. None	All	1.22 (0.57,2.59)	0.605
			Officer	1.81 (0.50,6.57)	0.366
			Enlisted Flyer	1.27 (0.35,4.58)	0.715
			Enlisted Groundcrew	0.69 (0.16,2.87)	0.607

--: Relative risk, confidence interval, and p-value are not presented because of the sparse number of participants with abnormalities.

Table G-22. Summary of Adjusted Results for Polytomous Variables – Model 2 (Ranch Hands: Log_2 (Initial Dioxin))

Table Ref.	Clinical Parameter	Contrast	Adj. Relative Risk (95% C.I.)	p-Value
11-28	Polyneuropathy Severity Index	Moderate vs. None or Mild	1.52 (1.02,2.28)	0.042
		Severe vs. None or Mild	0.87 (0.24,3.20)	0.832
13-48	α-1-Antitrypsin	Low vs. Normal	0.75 (0.30,1.84)	0.526
		High vs. Normal	0.80 (0.21,3.00)	0.735
15-4	RBC Count	Low vs. Normal	0.95 (0.64,1.41)	0.804
		High vs. Normal	0.88 (0.39,1.99)	0.751
15-6	WBC Count	Low vs. Normal	0.61 (0.38,0.99)	0.043
		High vs. Normal	0.83 (0.54,1.27)	0.395
15-8	Hemoglobin	Low vs. Normal	0.85 (0.61,1.20)	0.364
		High vs. Normal	1.04 (0.17,6.53)	0.966
15-10	Hematocrit	Low vs. Normal	1.10 (0.66,1.85)	0.714
		High vs. Normal	1.07 (0.17,6.61)	0.942
15-12	Platelet Count	Low vs. Normal	0.69 (0.35,1.37)	0.290
		High vs. Normal	0.67 (0.16,2.88)	0.590
16-5	Diabetic Severity	No Treatment vs. Nondiabetic	1.29 (0.93,1.78)	0.121
		Diet Only vs. Nondiabetic	1.25 (0.74,2.11)	0.411
		Oral Hypoglycemic vs. Nondiabetic	1.41 (0.98,2.01)	0.062
		Requiring Insulin vs. Nondiabetic	2.47 (1.43,4.25)	0.001
16-10	Thyroid Stimulating Hormone	Low vs. Normal	1.62 (0.82,3.20)	0.161
		High vs. Normal	1.29 (0.90,1.85)	0.169
16-21	Serum Insulin	Low vs. Normal	0.97 (0.65,1.47)	0.901
		High vs. Normal	1.15 (0.93,1.43)	0.182
18-11	Loss of Vital Capacity	Mild vs. None	0.91 (0.66,1.24)	0.539
		Moderate or Severe vs. None	1.02 (0.35,2.99)	0.973
18-12	Obstructive Abnormality	Mild vs. None	0.86 (0.72,1.02)	0.082
		Moderate vs. None	0.98 (0.67,1.42)	0.902
		Severe vs. None	0.63 (0.28,1.44)	0.276

Note: Relative risk for a twofold increase in initial dioxin.

Table G-23. **Summary of Adjusted Results for Polytomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category)**

Table Ref.	Clinical Parameter	Contrast	Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value
11-28	Polyneuropathy Severity Index	Moderate vs. None or Mild	Comparison	1,145		
			Background RH	358	1.29 (0.45,3.70)	0.641
			Low RH	225	2.35 (0.90,6.09)	0.079
			High RH	225	3.06 (1.16,8.11)	0.024
			Low plus High RH	450	2.68 (1.22,5.90)	0.014
		Severe vs. None or Mild	Comparison	1,145		
			Background RH	358	2.59 (0.15,43.89)	0.511
			Low RH	225	7.43 (0.62,89.56)	0.114
			High RH	225	9.83 (0.52,186.07)	0.128
			Low plus High RH	450	8.55 (0.77,94.34)	0.080
13-48	α-1-Antitrypsin	Low vs. Normal	Comparison	1,193		
			Background RH	374	0.78 (0.30,2.01)	0.602
			Low RH	235	0.76 (0.17,3.35)	0.712
			High RH	238	1.41 (0.28,7.06)	0.677
			Low plus High RH	473	1.03 (0.32,3.31)	0.955
		High vs. Normal	Comparison	1,193		
			Background RH	374	2.76 (0.74,10.35)	0.131
			Low RH	235	1.16 (0.13,10.62)	0.895
			High RH	238	2.64 (0.43,16.23)	0.295
			Low plus High RH	473	1.75 (0.36,8.53)	0.486
15-4	RBC Count	Low vs. Normal	Comparison	1,210		
			Background RH	380	1.07 (0.61,1.86)	0.818
			Low RH	238	0.92 (0.48,1.78)	0.809
			High RH	239	1.04 (0.49,2.23)	0.917
			Low plus High RH	477	0.98 (0.57,1.68)	0.942

Table G-23. Summary of Adjusted Results for Polytomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Contrast	Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value
15-4	RBC Count (continued)	High vs. Normal	Comparison	1,210		
			Background RH	380	0.25 (0.03,1.99)	0.192
			Low RH	238	0.54 (0.12,2.48)	0.431
			High RH	239	1.16 (0.31,4.42)	0.827
			Low plus High RH	477	0.79 (0.27,2.33)	0.676
15-6	WBC Count	Low vs. Normal	Comparison	1,210		
			Background RH	380	1.16 (0.70,1.93)	0.564
			Low RH	238	1.67 (0.96,2.91)	0.070
			High RH	239	0.64 (0.26,1.56)	0.326
			Low plus High RH	477	1.03 (0.59,1.81)	0.907
		High vs. Normal	Comparison	1,210		
			Background RH	380	0.86 (0.43,1.71)	0.660
			Low RH	238	0.82 (0.36,1.90)	0.650
			High RH	239	1.09 (0.53,2.24)	0.825
			Low plus High RH	477	0.95 (0.52,1.72)	0.855
15-8	Hemoglobin	Low vs. Normal	Comparison	1,210		
			Background RH	380	1.44 (0.91,2.29)	0.118
			Low RH	238	0.96 (0.54,1.70)	0.886
			High RH	239	0.90 (0.48,1.69)	0.735
			Low plus High RH	477	0.93 (0.59,1.47)	0.746
		High vs. Normal	Comparison	1,210		
			Background RH	380	1.01 (0.20,5.14)	0.987
			Low RH	238	--	--
			High RH	239	0.69 (0.08,6.00)	0.735
			Low plus High RH	477	--	--

Table G-23. Summary of Adjusted Results for Polytomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Contrast	Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value
15-10	Hematocrit	Low vs. Normal	Comparison	1,210		
			Background RH	380	1.00 (0.44,2.28)	0.998
			Low RH	238	0.78 (0.29,2.07)	0.615
			High RH	239	1.01 (0.37,2.77)	0.980
			Low plus High RH	477	0.89 (0.42,1.89)	0.757
		High vs. Normal	Comparison	1,210		
			Background RH	380	--	--
			Low RH	238	--	--
			High RH	239	0.98 (0.10,9.53)	0.986
			Low plus High RH	477	--	--
15-12	Platelet Count	Low vs. Normal	Comparison	1,204		
			Background RH	378	1.40 (0.73,2.70)	0.310
			Low RH	237	0.79 (0.33,1.92)	0.604
			High RH	238	0.26 (0.06,1.11)	0.068
			Low plus High RH	475	0.45 (0.19,1.09)	0.078
		High vs. Normal	Comparison	1,204		
			Background RH	378	0.86 (0.16,4.61)	0.858
			Low RH	237	--	--
			High RH	238	3.37 (0.50,22.63)	0.211
			Low plus High RH	475	--	--
16-5	Diabetic Severity	No Treatment vs. Nondiabetic	Comparison	1,183		
			Background RH	375	0.92 (0.51,1.65)	0.771
			Low RH	232	0.95 (0.50,1.80)	0.878
			High RH	238	1.58 (0.89,2.81)	0.122
			Low plus High RH	470	1.23 (0.77,1.95)	0.385

Table G-23. Summary of Adjusted Results for Polytomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Contrast	Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value
16-5	Diabetic Severity (continued)	Diet Only vs. Nondiabetic	Comparison	1,183		
			Background RH	375	1.24 (0.47,3.30)	0.661
			Low RH	232	1.55 (0.55,4.34)	0.408
			High RH	238	2.32 (0.88,6.12)	0.089
			Low plus High RH	470	1.90 (0.87,4.15)	0.108
		Oral Hypoglycemic vs. Nondiabetic	Comparison	1,183		
			Background RH	375	0.28 (0.11,0.71)	0.008
			Low RH	232	0.89 (0.46,1.71)	0.726
			High RH	238	1.17 (0.63,2.18)	0.624
			Low plus High RH	470	1.02 (0.63,1.65)	0.931
		Requiring Insulin vs. Nondiabetic	Comparison	1,183		
			Background RH	375	1.42 (0.59,3.45)	0.435
			Low RH	232	2.41 (1.00,5.82)	0.050
			High RH	238	3.46 (1.36,8.81)	0.009
			Low plus High RH	470	2.90 (1.40,5.99)	0.004
16-10	TSH	Low vs. Normal	Comparison	1,161		
			Background RH	365	2.33 (0.79,6.87)	0.125
			Low RH	233	0.52 (0.06,4.15)	0.536
			High RH	233	1.51 (0.39,5.91)	0.550
			Low plus High RH	466	0.89 (0.24,3.33)	0.858
		High vs. Normal	Comparison	1,161		
			Background RH	365	1.43 (0.78,2.62)	0.244
			Low RH	233	0.98 (0.43,2.24)	0.963
			High RH	233	1.58 (0.74,3.35)	0.236
			Low plus High RH	466	1.24 (0.68,2.28)	0.481

Table G-23. Summary of Adjusted Results for Polytomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Contrast	Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value
16-21	Serum Insulin	Low vs. Normal	Comparison	987		
			Background RH	338	0.90 (0.61,1.31)	0.573
			Low RH	183	0.82 (0.47,1.44)	0.496
			High RH	181	0.55 (0.29,1.08)	0.081
			Low plus High RH	364	0.68 (0.43,1.07)	0.093
		High vs. Normal	Comparison	987		
			Background RH	338	0.99 (0.74,1.34)	0.971
			Low RH	183	1.00 (0.70,1.44)	0.994
			High RH	181	0.94 (0.65,1.37)	0.759
			Low plus High RH	364	0.97 (0.74,1.28)	0.843
18-11	Loss of Vital Capacity	Mild vs. None	Comparison	1,210		
			Background RH	380	1.28 (0.82,1.99)	0.284
			Low RH	237	0.71 (0.41,1.24)	0.235
			High RH	243	0.75 (0.43,1.32)	0.325
			Low plus High RH	480	0.73 (0.48,1.12)	0.151
		Moderate or Severe vs. None	Comparison	1,210		
			Background RH	380	1.44 (0.54,3.81)	0.468
			Low RH	237	0.34 (0.07,1.57)	0.165
			High RH	243	0.47 (0.10,2.17)	0.337
			Low plus High RH	480	0.40 (0.13,1.25)	0.115

Table G-23. Summary of Adjusted Results for Polytomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Contrast	Dioxin Category	n	Adj. Relative Risk (95% C.I.)	p-Value
18-12	Obstructive Abnormality	Mild vs. None	Comparison	1,210		
			Background RH	380	1.21 (0.93,1.58)	0.164
			Low RH	237	1.17 (0.85,1.60)	0.338
			High RH	243	0.74 (0.52,1.06)	0.096
			Low plus High RH	480	0.93 (0.72,1.20)	0.556
		Moderate vs. None	Comparison	1,210		
			Background RH	380	1.22 (0.73,2.04)	0.440
			Low RH	237	0.78 (0.40,1.52)	0.459
			High RH	243	0.76 (0.39,1.49)	0.429
			Low plus High RH	480	0.77 (0.46,1.28)	0.311
		Severe vs. None	Comparison	1,210		
			Background RH	380	1.64 (0.62,4.34)	0.323
			Low RH	237	1.75 (0.62,4.89)	0.289
			High RH	243	0.28 (0.03,2.26)	0.232
			Low plus High RH	480	0.69 (0.20,2.37)	0.557

--: Relative risk, confidence interval, and p-value are not presented because of the sparse number of participants with abnormalities.

Note: Relative risk and confidence interval relative to Comparisons.
RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background: (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table G-24. Summary of Adjusted Results for Polytomous Variables – Model 4 (Ranch Hands: Log_2 (1987 Dioxin + 1))

Table Ref.	Clinical Parameter	Contrast	Adj. Relative Risk (95% C.I.)	p-Value
11-28	Polyneuropathy Severity Index	Moderate vs. None or Mild	1.51 (1.09,2.09)	0.013
		Severe vs. None or Mild	1.48 (0.62,3.50)	0.376
13-48	α-1-Antitrypsin	Low vs. Normal	0.84 (0.52,1.37)	0.486
		High vs. Normal	0.75 (0.44,1.29)	0.302
15-4	RBC Count	Low vs. Normal	0.91 (0.69,1.21)	0.511
		High vs. Normal	1.10 (0.60,2.00)	0.764
15-6	WBC Count	Low vs. Normal	0.76 (0.59,0.98)	0.032
		High vs. Normal	0.93 (0.72,1.20)	0.570
15-8	Hemoglobin	Low vs. Normal	0.84 (0.68,1.04)	0.108
		High vs. Normal	0.52 (0.22,1.23)	0.135
15-10	Hematocrit	Low vs. Normal	0.97 (0.67,1.42)	0.894
		High vs. Normal	1.44 (0.38,5.40)	0.588
15-12	Platelet Count	Low vs. Normal	0.73 (0.49,1.10)	0.135
		High vs. Normal	0.84 (0.43,1.64)	0.619
16-5	Diabetic Severity	No Treatment vs. Nondiabetic	1.23 (0.96,1.58)	0.097
		Diet Only vs. Nondiabetic	1.49 (1.00,2.20)	0.048
		Oral Hypoglycemic vs. Nondiabetic	1.85 (1.37,2.49)	<0.001
		Requiring Insulin vs. Nondiabetic	1.38 (0.96,2.00)	0.084
16-10	TSH	Low vs. Normal	1.08 (0.64,1.83)	0.767
		High vs. Normal	0.97 (0.74,1.27)	0.832
16-21	Serum Insulin	Low vs. Normal	0.94 (0.76,1.17)	0.589
		High vs. Normal	1.03 (0.89,1.19)	0.685
18-11	Loss of Vital Capacity	Mild vs. None	0.80 (0.65,1.00)	0.046
		Moderate or Severe vs. None	0.87 (0.50,1.50)	0.605
18-12	Obstructive Abnormality	Mild vs. None	0.91 (0.80,1.04)	0.177
		Moderate vs. None	0.87 (0.67,1.12)	0.269
		Severe vs. None	0.78 (0.50,1.22)	0.272

Note: Relative risk for a twofold increase in 1987 dioxin.

APPENDIX H

APPENDIX H. ABBREVIATIONS AND ACRONYMS

A	adjusted analyses
Adj. Mean	adjusted mean
Adj. RR	adjusted relative risk
Adj. Slope	adjusted slope
AFHS	Air Force Health Study
Ah	aryl hydrocarbon
AIDS	acquired immunodeficiency syndrome
ALT	alanine aminotransferase
ANA	antinuclear antibody
AST	aspartate aminotransferase
C	Celsius
C	Comparison(s)
C	continuous analysis only
CAPI	computer-assisted personal interview
CDC	Centers for Disease Control and Prevention
CI	Cornell Index
C.I.	confidence interval
CMI	Cornell Medical Index
CNS	central nervous system
COV	covariate
cpm	counts per minute
CS	chi-square contingency table analysis (continuity-adjusted)
CV	coefficient of variation
D	discrete analysis only
D/C	discrete and continuous analyses for dependent variables; appropriate form for analysis (either discrete or continuous) for covariates
DEP	dependent variable
DNA	deoxyribonucleic acid
DXCAT	categorized dioxin
ECG	electrocardiograph or electrocardiogram
Est. RR	estimated relative risk
EXC	exclusion

FC	fully compliant at the baseline examination
FEFmax	forced expiratory flow maximum
FEV_1	forced expiratory volume in 1 second
FSH	follicle stimulating hormone
FTI	free thyroxine index
FVC	forced vital capacity
G	good result
GGT	gamma glutamyl transferase
GLM	general linear models analysis
GND	good result, measurable below limit of detection
GNQ	good result, measurable below limit of quantification
GSI	global severity index
HDL	high-density lipoprotein
HIV	human immunodeficiency virus
HRB	Halstead-Reitan Battery
ICD-9-CM	International Classification of Disease, 9th Edition, Clinical Modification
ICVI	intermittent claudication and vascular insufficiency
IL-2	Interleukin-2
IOM	Institute of Medicine
IQ	intelligence quotient
L	longitudinal analysis
LAB	1997 laboratory results
LBBB	left bundle branch block
LDH	lactic dehydrogenase
LH	luteinizing hormone
LR	logistic regression analysis
MCH	mean corpuscular hemoglobin
MCHC	mean corpuscular hemoglobin concentration
MCMI	Millon Clinical Multiaxial Inventory
MCV	mean corpuscular volume
MIL	Air Force military records
ml	milliliter

MLC	mixed lymphocyte culture
MMPI	Minnesota Multiphasic Personality Inventory
MR-V	medical records (verified)
MSK	mouse stomach kidney
NAS	National Academy of Sciences
NHL	non-Hodgkin's lymphoma
NIDDM	non-insulin-dependent diabetes mellitus
NIH	National Institutes of Health
NIOSH	National Institute for Occupational Safety and Health
NKC	natural killer cell
NORC	National Opinion Research Center
NR	no result
NS	new to study since the baseline examination (Chapter 5)
NS or ns	not significant ($p>0.10$)
NS* or ns*	marginally significant ($0.05<p\leq0.10$)
OMR	optical mark recognition
PA	posterior-anterior
PBS	phosphate-buffered saline
PC	partially compliant at the baseline examination
PCT	porphyria cutanea tarda
PE	physical examination
PHA	phytohemagglutinin
ppq	parts per quadrillion
ppt	parts per trillion
PR	polytomous logistic regression analysis
PSA	prostate-specific antigen
PSDI	positive symptom distress index
PST	positive symptom total
PTSD	post-traumatic stress disorder
PWM	pokeweed mitogen
QA	quality assurance
QC	quality control
QRC	Quality Review Committee
Q-SR	health questionnaire (self-reported)

Appendix H. Abbreviations and Acronyms (Continued)

R	refusal at the baseline examination
R^2	coefficient of determination
RBBB	right bundle branch block
RBC	red blood cell
RH	Ranch Hand(s)
RIA	radioimmunoassay
RPM	revolutions per minute
RR	relative risk
RVN	Republic of Vietnam
SAIC	Science Applications International Corporation
SCL-90-R	Symptom Checklist-90-Revised
SEA	Southeast Asia
ST	survival time analysis
Std. Error	standard error
STS	soft tissue sarcoma
T_3	triiodothyronine
T_4	serum thyroxine
TCDD	2,3,7,8-tetrachlorodibenzo-p-dioxin
TLC	total lymphocyte count
TSH	thyroid stimulating hormone
2,4-D	dichlorophenoxyacetic acid
2,4,5-T	2,4,5-trichlorophenoxyacetic acid
U	unadjusted analyses
UNL	unlocatable at the baseline examination
USAF	United States Air Force
VA	Veterans' Administration
VES	Vietnam Experience Study
VU	vibrational units
WAIS	Wechsler Adult Intelligence Scale
WBC	white blood cell